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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases

NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:53:58 ON 09 FEB 2007

=> eg
EG IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> fil ref
'REF' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'HOME'
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available. If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 09:54:08 ON 09 FEB 2007
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 7 FEB 2007 HIGHEST RN 919834-45-0
DICTIONARY FILE UPDATES: 7 FEB 2007 HIGHEST RN 919834-45-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

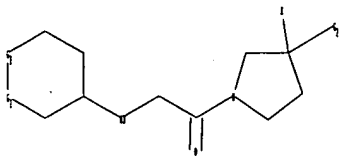
Please note that search-term pricing does apply when conducting SmartSELECT searches.

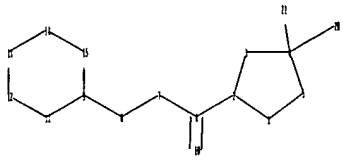
REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10507005s1.str

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chain nodes :
6 7 8 10 20 21
ring nodes :
1 2 3 4 5 9 11 12 13 14 15
chain bonds :
2-6 4-20 4-21 6-7 6-10 7-8 8-9
ring bonds :
1-2 1-5 2-3 3-4 4-5 9-11 9-15 11-12 12-13 13-14 14-15
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 4-5 4-20 4-21 6-7 6-10 7-8 8-9 9-11 9-15 11-12
12-13 13-14 14-15
isolated ring systems :
containing 1 :

G1:C,N

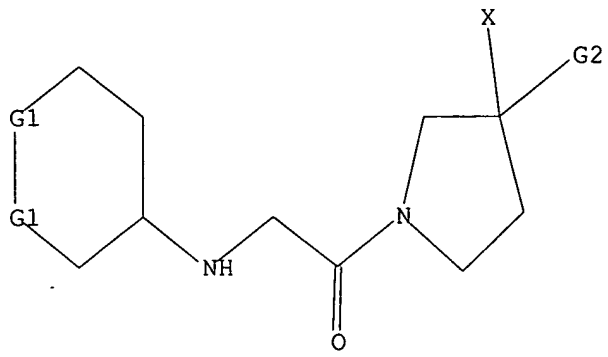
G2:H,X

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:Atom 10:CLASS
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 20:CLASS 21:CLASS

L1 STRUCTURE UPLOADED

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=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 C,N

G2 H,X

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 09:54:35 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 780 TO ITERATE

100.0% PROCESSED 780 ITERATIONS 39 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 13925 TO 17275
PROJECTED ANSWERS: 406 TO 1154

L2 39 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 09:54:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 16361 TO ITERATE

100.0% PROCESSED 16361 ITERATIONS 626 ANSWERS
SEARCH TIME: 00.00.01

L3 626 SEA SSS FUL L1

=> fil hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 172.10 172.31

FILE 'HCAPLUS' ENTERED AT 09:54:48 ON 09 FEB 2007
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FILE COVERS 1907 - 9 Feb 2007 VOL 146 ISS 8
FILE LAST UPDATED: 8 Feb 2007 (20070208/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 23 L3

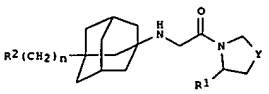
=> d ed ibib abs hitstr 1-23

L4 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 31 Aug 2006
ACCESSION NUMBER: 2006:886440 HCAPLUS
DOCUMENT NUMBER: 145:292604
TITLE: Preparation of adamantane derivatives as dipeptidyl peptidase IV inhibitors, and pharmaceutical compositions containing them
INVENTOR(S): Gopalan, Balasubramanian; Thomas, Abraham; Shah, Daisy
Manish
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals S.A., Switz.
SOURCE: PCT Int. Appl., 81pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

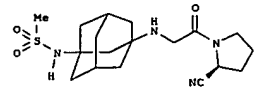
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006090244	A1	20060831	WO 2006-IB363	20060222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			IN 2005-MU194	A 20050222
			US 2005-656233P	P 20050224

OTHER SOURCE(S): CASREACT 145:292604; MARPAT 145:292604
GI

L4 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I

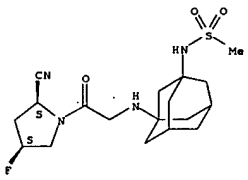


II

AB Title compds. I [Y = S(O)m, CH2, CHF, or CF2; R1 = H, CN, CO2H, or an isostere of a carboxylic acid; R2 = (un)substituted alkenyl, alkynyl, cycloalkyl, etc.; n = 0-3], and their pharmaceutically acceptable salts, are prepared as dipeptidyl peptidase IV (DPP-IV) inhibitors. Thus, e.g., II was prepared by N-alkylation of N-(3-amino-1-adamantyl)methanesulfonamide (preparation given) with (2S)-1-(2-chloroacetyl)-2-pyrrolidinecarbonitrile. In DPP-IV inhibition assays using human recombinant DPP-IV enzyme, e.g., II demonstrated an IC50 value of 21.78 nM. Further disclosed are methods for treating disorders mediated by DPP-IV inhibition, such as diabetes, especially Type II diabetes.
IT 908290-45-9P 908290-49-3P 908290-53-9P
908290-63-1P 908290-69-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of adamantane derivs. as dipeptidyl peptidase IV inhibitors)
RN 908290-45-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[3-[(methylsulfonyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

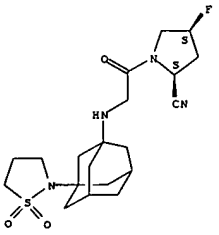
Absolute stereochemistry.

L4 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 908290-49-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-(1,1-dioxido-2-isothiazolidinyl)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

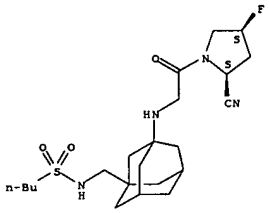
Absolute stereochemistry.



RN 908290-53-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-[[(butylsulfonyl)amino]methyl]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

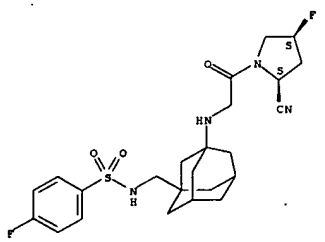
Absolute stereochemistry.

L4 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 908290-63-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[3-[[[(4-fluorophenyl)sulfonyl]amino]methyl]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

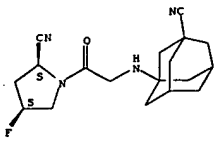
Absolute stereochemistry.



RN 908290-69-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-cyanotricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

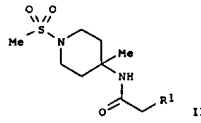
L4 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 15 Jun 2006
ACCESSION NUMBER: 2006:558355 HCAPLUS
DOCUMENT NUMBER: 145:45956
TITLE: Process for producing 1-methanesulfonyl-4-methylpiperidine-4-amine
INVENTOR(S): Sugimori, Toshiyuki; Sano, Kuniyuki; Komenoi, Kousuke
PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006062063	A1	20060615	WO 2005-JP22299	20051205

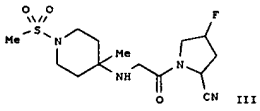
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2004-355904 A 20041208

OTHER SOURCE(S): MARPAT 145:45956
GI



II

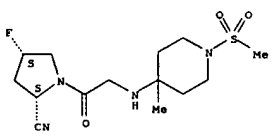


III

L4 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB Process for the preparation of 1-methanesulfonyl-4-methylpiperidine-4-amine (I) and salts thereof from compds. II [R1 = H, halo, OH] were prepared For example, to a solution of 1-methanesulfonyl-4-methylpiperidin-4-ol (10.00 g) in acetic acid (15 mL) were added sulfuric acid (10 mL) and chloroacetonitrile (5.08 g) at ≤20 °C, then reaction was stirred for 3 days. Aqueous work-up, removal of solvent under reduced pressure followed by treatment with n-butanol (60 mL), water (10 mL) and concentrated HCl (10 mL) at 100 °C for 13 h afforded 1-methanesulfonyl-4-methylpiperidine-4-amine·1HCl·1H2O (7.81 g), which was converted to (2S,4S)-III by reacting with (2S,4S)-1-(chloroacetyl)-4-fluoropyrrolidine-2-carbonitrile. Of note, compound I is a useful intermediate for preparing DPP-IV inhibitor III.
IT 651055-25-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of piperidine compound containing chiral pyrrolidine moiety via N-alkylation of 1-(methanesulfonyl)-4-methylpiperidine-4-amine with (2S,4S)-1-(chloroacetyl)-4-fluoropyrrolidine-2-carbonitrile)
RN 651055-25-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-methyl-1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

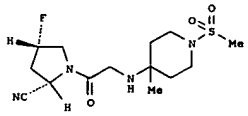
L4 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 27 Apr 2006
ACCESSION NUMBER: 2006:380982 HCAPLUS
DOCUMENT NUMBER: 144:412359
TITLE: Process for producing 2-cyano-4-fluoropyrrolidine derivative
INVENTOR(S): Yamashita, Yohei; Hayakawa, Masahiko; Nigawara, Takahiro
PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006043595	A1	20060427	WO 2005-JP19209	20051019

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2004-307520 A 20041022

OTHER SOURCE(S): MARPAT 144:412359
GI



I

AB A novel process for producing 4-fluoro-1-[[[4-methyl-1-(methanesulfonyl)piperidin-4-yl]amino]acetyl]pyrrolidine-2-carbonitrile (I) or a salt thereof and 2-aminocarbonyl-4-fluoropyrrolidine derivative as an intermediate for the compound I is disclosed. The compound I is useful as a medicine, especially a dipeptidyl peptidase IV inhibitor, for the treatment and/or prevention of type I diabetes, type II diabetes, insulin resistance disease, or obesity. According to the process, the precursor is expected to crystallize out and this is expected to lead to an improvement in yield

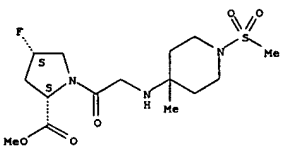
L4 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
and avoidance of column purifn. The precursor has improved lipid soly. and, as a result, has improved soly. in solvents other than halogenated ones. Use of these halogenated solvents is expected to be avoidable. Thus, 5.0 g (2S,4S)-1-[[[tert-butoxycarbonyl][4-methyl-1-(methanesulfonyl]piperidin-4-yl]amino]acetyl]-4-fluoropyrrolidine-2-carboxylic acid was treated with 10 mL iso-Pr acetate and 1.8 mL Et3N, dissolved under stirring, and treated with a soln. of 1.25 mL Et chlorocarbonate in iso-Pr acetate (25 mL) at ≤5° under ice-cooling. The reaction mixt. was added to a mixt. of 15 mL 25% aq. NH3 soln. and 15 mL iso-Pr acetate at ≤6° under ice-cooling and stirred at ≤5° for 2 h to give, after workup and silica gel chromatog., 4.67 g tert-Bu [2-[(2S,4S)-2-(aminocarbonyl)-4-fluoropyrrolidin-1-yl]-2-oxoethyl][4-methyl-1-(methanesulfonyl)piperidin-4-yl]carbamate (II). II (2.0 g) was treated with 20 mL CH2Cl2, treated with 1.27 g p-toluenesulfonic acid monohydrate with heating at .apprx.40° under stirring for 2 h, and filtered to give 2.21 g (2S,4S)-4-fluoro-1-[[[4-methyl-1-(methanesulfonyl]piperidin-4-yl]amino]acetyl]pyrrolidine-2-carbonitrile p-toluenesulfonate monohydrate.

IT 884496-53-1P, (2S,4S)-4-Fluoro-1-[[[4-methyl-1-(methanesulfonyl)piperidin-4-yl]amino]acetyl]pyrrolidine-2-carboxylic acid methyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; process for producing 2-cyano-4-fluoropyrrolidine derivative via aminocarbonylfluoropyrrolidine derivative as dipeptidyl peptidase inhibitor)

RN 884496-53-1 HCAPLUS

CN L-Proline, N-[4-methyl-1-(methylsulfonyl)-4-piperidinyl]glycyl-4-fluoro-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



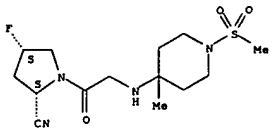
IT 651055-25-3P, (2S,4S)-4-Fluoro-1-[[[4-methyl-1-(methanesulfonyl)piperidin-4-yl]amino]acetyl]pyrrolidine-2-carbonitrile
884496-57-5P, (2S,4S)-4-Fluoro-1-[[[4-methyl-1-(methanesulfonyl)piperidin-4-yl]amino]acetyl]pyrrolidine-2-carbonitrile p-toluenesulfonate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

L4 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for producing 2-cyano-4-fluoropyrrolidine deriv. via aminocarbonylfluoropyrrolidine deriv. as dipeptidyl peptidase inhibitor)

RN 651055-25-3 HCAPLUS

CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-methyl-1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



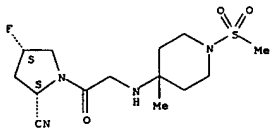
RN 884496-57-5 HCAPLUS

CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-methyl-1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)-, mono(4-methylbenzenesulfonate) (9CI)
(CA INDEX NAME)

CM 1

CRN 651055-25-3
CMF C14 H23 F N4 O3 S

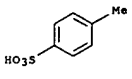
Absolute stereochemistry.



CM 2

CRN 104-15-4
CMF C7 H8 O3 S

L4 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 03 Feb 2006
ACCESSION NUMBER: 2006:103268 HCAPLUS
DOCUMENT NUMBER: 144:192098
TITLE: 1-Aminoacetyl-2-cyanopyrrolidine derivatives as dipeptidyl peptidase IV inhibitors and their preparation, pharmaceutical compositions, and use for treatment of diabetes
INVENTOR(S): Royalty, Susan Marie; Burns, James Ford; Scicinski, Jan Jozef; Foglesong, Robert James; Jagdmann, Gunnar Erik, Jr.; Griffin, Kellee Renee; Dyakonov, Tatyana; Middlemiss, David
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

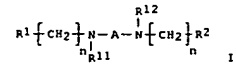
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006012441	A1	20060202	WO 2005-US25918	20050721

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

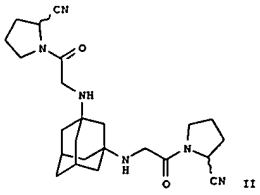
PRIORITY APPLN. INFO.: US 2004-590529P P 20040723
US 2004-634181P P 20041208
US 2004-634182P P 20041208

OTHER SOURCE(S): MARPAT 144:192098
GI

L4 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I



II

AB The invention relates to a series of compds. having formula I, which are useful as dipeptidyl peptidase IV (DPP-IV) inhibitors and for treating diabetes. Compds. of formula I wherein each n are independently 1 or 2; A is mono-, bi- or tricyclic carbocycle of 5 to 20 atoms where each bridge of the bicycle has at least one atom; R1 and R2 are independently heterocycloaminocarbonyl, etc.; R11 and R12 are independently H, alkylcarbonyl, alkoxycarbonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, or sulfone; and the pharmaceutically acceptable salts or prodrug thereof are claimed in this invention. Example compound (S,S)-II was prepared by alkylation of 1,3-diaminoadamantane with (S)-1-(2-chloroacetyl)pyrrolidine-2-carbonitrile. The invention compds. were evaluated for their DPP-IV inhibition activity and from the assay the IC50 values were determined Invention compound (S,S)-II has an IC50 of 5 nM against DPP-IV and showed 97 % inhibition of DPP-IV.

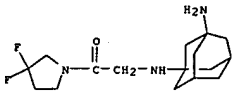
IT 875311-34-5P 875314-97-9P 875315-13-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoacetyl(cyano)pyrrolidines as dipeptidyl peptidase IV inhibitors and use for treatment of diabetes)

RN 875311-34-5 HCAPLUS
CN Pyrrolidine, 1-[[(3-aminotricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-3,3-difluoro- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

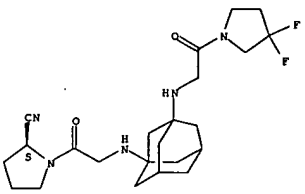
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

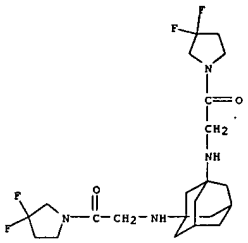


RN 875314-97-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-[[2-(3,3-difluoro-1-pyrrolidinyl)-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 875315-13-2 HCAPLUS
CN Pyrrolidine, 1,1'-(tricyclo[3.3.1.13,7]decane-1,3-diylbis[imino(1-oxo-2,1-ethanediyl)])bis[3,3-difluoro- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 03 Feb 2006
ACCESSION NUMBER: 2006:101144 HCAPLUS
DOCUMENT NUMBER: 144:192096
TITLE: 1-Aminoacetyl-2-cyanopyrrolidine derivatives as dipeptidyl peptidase IV inhibitors and their preparation, pharmaceutical compositions, and use for treatment of diabetes
INVENTOR(S): Royalty, Susan Marie; Burns, James Ford; Scicinski, Jan Jozef; Jagdmann, Gunnar Erik, Jr.; Foglesong, Robert James; Griffin, Kellee Renee; Dyakonov, Tatyana; Middlemiss, David
PATENT ASSIGNEE(S): Jagdmann, Jr., Gunnar Erik, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

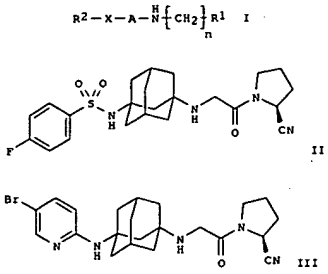
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006012395	A2	20060202	WO 2005-US25837	20050721
WO 2006012395	A3	20060504		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:	US 2004-590541P	P	20040723
	US 2004-634362P	P	20041208

OTHER SOURCE(S): MARPAT 144:192096
GI

L4 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



II

III

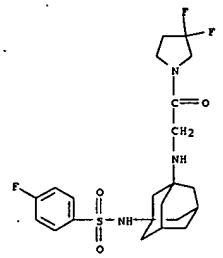
AB The invention relates to a series of compds. of formula I, which are useful as DPP-IV inhibitors for treatment of diabetes. Compds. of formula I wherein C is NH and derivs. or O; n is 1 or 2; A is bicyclic or tricyclic carbocycle of 5 to 20 atoms where each bridge of the bicycle has at least one atom; R1 is (un)substituted heterocycloaminocarbonyl, etc.; R2 is R4SO2, R5SO2NHCO, H2NSO2 and derivs.; or (un)substituted heterocyclic group; where R4 is haloalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl(alkyl), or heterocyclo(alkyl); R5 is alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl(alkyl), or heterocyclo(alkyl); and the corresponding pharmaceutically acceptable salts or prodrug thereof are claimed in this invention. Example compds. II was prepared by sulfonylation of (S)-1-[(3-amino-1-adamantyl)amino]acetyl-2-cyanopyrrolidine with 4-fluorophenylsulfonyl chloride to give compound II. All the example compds., in this invention, were evaluated for their dipeptidyl peptidase IV (DPP-IV) inhibitory activity and the IC50 values were determined from the assay. From the assay the IC50 values were determined Example compound II showed an IC50 value of 46 nM, and compound III showed 99 % and 96 % inhibition of DPP-IV at 1 μM and 100 nM concentration, resp.

IT 875310-73-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoacetyl(cyano)pyrrolidines as dipeptidyl peptidase IV inhibitors and use for treatment of diabetes)

RN 875310-73-9 HCAPLUS

CN Pyrrolidine, 3,3-difluoro-1-[[[3-[[(4-fluorophenyl)sulfonyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

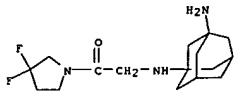
L4 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 875311-34-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminoacetyl(cyano)pyrrolidines as dipeptidyl peptidase IV inhibitors and use for treatment of diabetes)

RN 875311-34-5 HCAPLUS

CN Pyrrolidine, 1-[[(3-aminotricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-3,3-difluoro- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 09 Dec 2005

ACCESSION NUMBER: 2005:1292333 HCAPLUS

DOCUMENT NUMBER: 144:36259

TITLE: Preparation of piperidine compounds containing pyrrolidine moiety as DPP-IV inhibitors

INVENTOR(S): Hayakawa, Masahiko; Nakano, Ryosuke; Furutani, Masako

PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan

SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

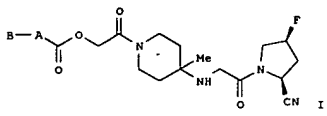
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005116012	A1	20051208	WO 2005-JP7770	20050425
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2564668	A1	20051208	CA 2005-2564668	20050425
EP 1741710	A1	20070110	EP 2005-734744	20050425
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: JP 2004-130674 A 20040427
WO 2005-JP7770 W 20050425

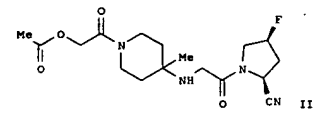
OTHER SOURCE(S): CASREACT 144:36259; MARPAT 144:36259

GI

L4 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I



II

AB Title compds. I [A = single bond, O, S, etc.; B = alkyl, alkenyl, alkynyl, etc.] were prepared For example, acetylation of (2S,4S)-4-fluoro-1-[[(1-glycoloyl-4-methylpiperidin-4-yl)amino]acetyl]pyrrolidine-2-carbonitrile monohydrochloride followed by treatment with fumaric acid afforded compound II·fumaric acid. In DPP4 inhibition assays, the IC50 value of compound II·fumaric acid was 15.0 nM. Compds. I are claimed useful for the treatment of diabetes, obesity, etc.

IT 870765-47-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidine compds. containing pyrrolidine moiety as DPP4 inhibitors for treatment of diabetes, obesity, etc.)

RN 870765-47-2 HCAPLUS

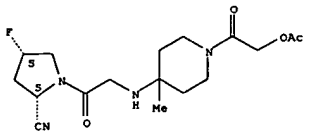
CN 4-Piperidinamine, 1-[(acetyloxy)acetyl]-N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-4-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 870765-46-1
CMF C17 H25 F N4 O4

Absolute stereochemistry.

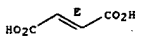
L4 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

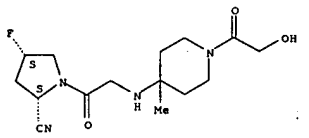
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



IT 870765-45-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperidine compds. containing pyrrolidine moiety as DPP4
inhibitors for treatment of diabetes, obesity, etc.)
RN 870765-45-0 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(hydroxyacetyl)-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

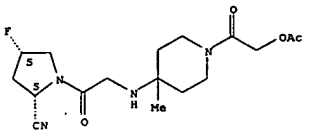


● HCl

IT 870765-46-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidine compds. containing pyrrolidine moiety as DPP4

L4 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
inhibitors for treatment of diabetes, obesity, etc.)
RN 870765-46-1 HCAPLUS
CN 4-Piperidinamine, 1-[(acetyloxy)acetyl]-N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



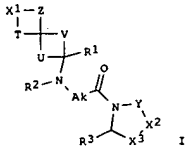
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 23 Nov 2005
ACCESSION NUMBER: 2005:1235661 HCAPLUS
DOCUMENT NUMBER: 143:477960
TITLE: Pyrrolidine and thiazolidine derivatives, their preparation and their use as dipeptidyl peptidase IV (DPP IV) inhibitors in the treatment of hyperglycemia and diabetes type II
INVENTOR(S): De Nanteuil, Guillaume; Benoist, Alain; Combettes, Murielle; Harley, Elizabeth
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

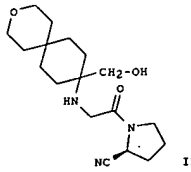
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1598350	A1	20051123	EP 2005-291066	20050518
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
FR 2870538	A1	20051125	FR 2004-5454	20040519
FR 2870538	B1	20060714		
SG 117551	A1	20051229	SG 2005-2766	20050504
CA 2506491	A1	20051119	CA 2005-2506491	20050505
US 2005261501	A1	20051124	US 2005-131510	20050518
NZ 540108	A	20060428	NZ 2005-540108	20050518
KR 2006048007	A	20060518	KR 2005-41742	20050518
NO 2005002414	A	20051121	NO 2005-2414	20050519
AU 2005202180	A1	20051208	AU 2005-202180	20050519
JP 2005350456	A	20051222	JP 2005-146186	20050519
BR 2005001769	A	20060110	BR 2005-1769	20050519
CN 1721417	A	20060118	CN 2005-10087845	20050519
PRIORITY APPLN. INFO.:			FR 2004-5454 A	20040519

OTHER SOURCE(S): MARPAT 143:477960
GI

L4 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



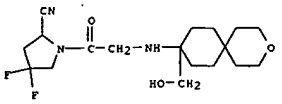
I



II

AB Title compds. I [X1 = CH2 and derivs., S, SO, SO2, NH and derivs.; Z = (CH2)m1; m1 = 0-4; T = (CH2)m2; m2 = 1-4; V = (CH2)n1; U = (CH2)n2; n1, n2
= independently 1-3; R1 = H, CO2H, alkoxycarbonyl, etc.; R2 = H, alkyl; Ak
= (un)substituted alkylene; Y = (CH2)p; p = 0-2; R3 = H, CN; X2, X3 = independently S, SO, SO2, CH2 and derivs.; their optical isomers when they
exist; and their acid addition salts] were prepared as dipeptidyl peptidase IV
(DPP IV) inhibitors. E.g., a 7-step synthesis from tetrahydro-2H-pyran-4-
carboxaldehyde and Me vinyl ketone, was given for pyrrolidine II (intermediates not isolated). II inhibited DPP IV with IC50 =76.1 nM. Thus, I and their compns. are useful in the treatment of hyperglycemia and
diabetes type II (no data).
IT 869769-64-2P, 4,4-Difluoro-1-{[[9-(hydroxymethyl)-3-oxaspiro[5.5]undecan-9-yl]amino]acetyl]-2-pyrrolidinecarbonitrile
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical
process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(drug candidate; preparation of pyrrolidines and thiazolidines as dipeptidyl
peptidase IV inhibitors and their use in treatment of hyperglycemia and
diabetes type II)
RN 869769-64-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-{[[9-(hydroxymethyl)-3-oxaspiro[5.5]undec-9-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

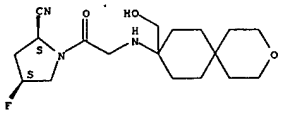
L4 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 869769-51-7P, (2S,4S)-4-Fluoro-1-[[[9-(hydroxymethyl)-3-oxaspiro[5.5]undecan-9-yl]amino]acetyl]-2-pyrrolidinecarbonitrile 869769-52-8P, (2S)-4,4-Difluoro-1-[[[9-(hydroxymethyl)-3-oxaspiro[5.5]undecan-9-yl]amino]acetyl]-2-pyrrolidinecarbonitrile 869769-56-2P 869769-57-3P, [9-[[2-Oxo-2-(3,3,4,4-tetrafluoro-1-pyrrolidinyl)ethyl]amino]-3-oxaspiro[5.5]undecan-9-yl]methanol 869769-66-4P, (2R)-4,4-Difluoro-1-[[[9-(hydroxymethyl)-3-oxaspiro[5.5]undecan-9-yl]amino]acetyl]-2-pyrrolidinecarbonitrile
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrrolidines and thiazolidines as dipeptidyl peptidase IV inhibitors and their use in treatment of hyperglycemia and diabetes type II)

RN 869769-51-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[9-(hydroxymethyl)-3-oxaspiro[5.5]undec-9-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

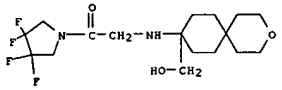
Absolute stereochemistry.



RN 869769-52-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[9-(hydroxymethyl)-3-oxaspiro[5.5]undec-9-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

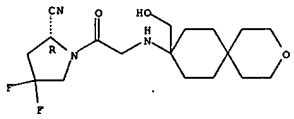
Absolute stereochemistry.

L4 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



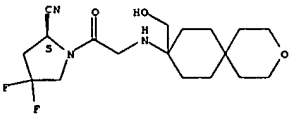
RN 869769-66-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[9-(hydroxymethyl)-3-oxaspiro[5.5]undec-9-yl]amino]acetyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

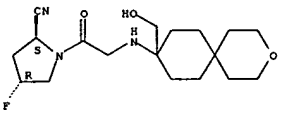


RN 869769-56-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[9-(hydroxymethyl)-3-oxaspiro[5.5]undec-9-yl]amino]acetyl]-, (2S,4R)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 869769-55-1
CMF C18 H28 F N3 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



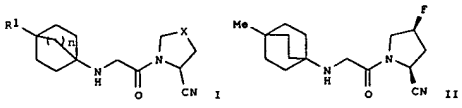
RN 869769-57-3 HCAPLUS
CN Pyrrolidine, 3,3,4,4-tetrafluoro-1-[[[9-(hydroxymethyl)-3-oxaspiro[5.5]undec-9-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 08 Sep 2005
ACCESSION NUMBER: 2005:977014 HCAPLUS
DOCUMENT NUMBER: 143:286277
TITLE: Preparation of pyrrolidine compounds having bicyclic amide moiety as DPP-IV inhibitors
INVENTOR(S): Fukuda, Yasumichi; Asahina, Yoshikazu; Yokota, Kazuya; Murakami, Koji; Ide, Tomohiro
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005082847	A1	20050909	WO 2005-JP2806	20050222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2557275	A1	20050909	CA 2005-2557275	20050222
EP 1719757	A1	20061108	EP 2005-719381	20050222
R: DE, FR, GB, IT				

PRIORITY APPLN. INFO.: JP 2004-53305 A 20040227
WO 2005-JP2806 W 20050222

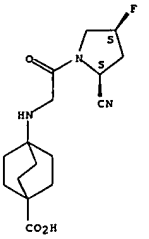
OTHER SOURCE(S): MARPAT 143:286277
GI



AB Title compds. represented by the formula I [wherein R1= H, halo, carboxyl, (hydroxy)alkyl, (un)substituted aryl; X = CH2, CHF, CF2, CHOH, S or O; n = 1-3; and pharmacol. acceptable salts thereof] were prepared as DPP-IV (dipeptidyl peptidase IV) inhibitors. For example, substitution of

L4 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
4-amino-1-methylbicyclo[2.2.2]octane with (2S,4S)-1-(2-bromoacetyl)-4-fluoropyrrolidine-2-carbonitrile gave II. II showed inhibition of DPP-IV with an IC50 value of 0.25 nmol/L. Thus, I are useful as DPP-IV inhibitors for the treatment of DPP-IV mediated diseases, such as diabetes.
IT 862501-98-2P 864063-49-0P 864063-51-4P
864063-53-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidine compds. having bicyclic amide moiety as DPP-IV
inhibitors for the treatment of diabetes)
RN 862501-98-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

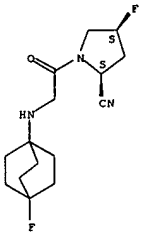
Absolute stereochemistry.



RN 864063-49-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(4-methylbicyclo[2.2.2]oct-1-yl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

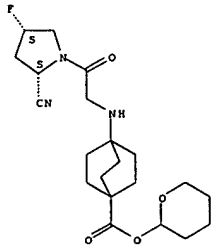
Absolute stereochemistry.

L4 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



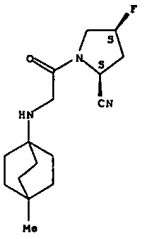
IT 862501-64-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrolidine compds. having bicyclic amide moiety as DPP-IV
inhibitors for the treatment of diabetes)
RN 862501-64-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, tetrahydro-2H-pyran-2-yl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



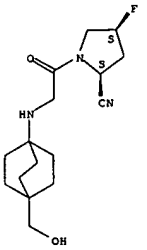
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 864063-51-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile,
4-fluoro-1-[[[4-(hydroxymethyl)bicyclo[2.2.2]oct-1-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 864063-53-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(4-fluorobicyclo[2.2.2]oct-1-yl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

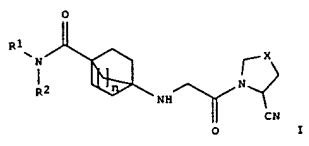
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 26 Aug 2005
ACCESSION NUMBER: 2005:902853 HCAPLUS
DOCUMENT NUMBER: 143:248276
TITLE: Preparation of pyrrolidine compounds having bicyclic amide moiety as DPP-IV inhibitors
INVENTOR(S): Fukuda, Yasumichi; Asahina, Yoshikazu; Katayama, Satoru; Shibue, Taku; Murakami, Koji; Ide, Tomohiro
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 198 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077900	A1	20050825	WO 2005-JP2389	20050217
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005212073	A1	20050825	AU 2005-212073	20050217
CA 2554378	A1	20050825	CA 2005-2554378	20050217
EP 1717225	A1	20061102	EP 2005-710289	20050217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				

PRIORITY APPLN. INFO.: JP 2004-41407 A 20040218
WO 2005-JP2389 W 20050217

OTHER SOURCE(S): MARPAT 143:248276
GI



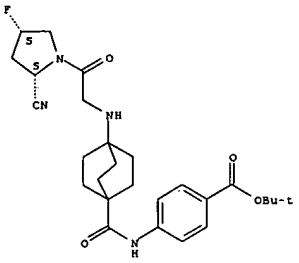
AB Title compds. I [R1, R2 = H, (un)substituted alkyl, etc.; X = CH2, etc.; n = 1-3) were prepared For example, N-alkylation of 4-aminobicyclo[2.2.2]octane-1-carboxamide, e.g., prepared from bicyclo[2.2.2]octane-1,4-dicarboxylic acid monomethyl ester in 4 steps, with (2S,4S)-1-(2-bromoacetyl)-4-fluoropyrrolidine-2-carbonitrile afforded

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(2S,4S)-1-[[(4-carbamoylbicyclo[2.2.2]oct-1-yl)amino]acetyl]-4-fluoropyrrolidine-2-carbonitrile (II). In DPP-IV (dipeptidyl peptidase IV) inhibition assays (in vitro), compd. II exhibited the IC50 value of 0.89 nmol/mL. Compds. I are claimed useful for the treatment of diabetes.

IT 863303-61-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrrolidine compds. having bicyclic amide moiety as DPP-IV inhibitors for the treatment of diabetes)

RN 863303-61-1 HCAPLUS
CN Benzoic acid, 4-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



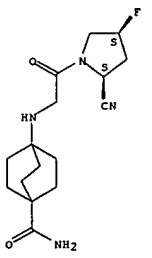
IT 863302-11-8P 863302-14-1P 863302-15-2P
863302-16-3P 863302-17-4P 863302-18-5P
863302-19-6P 863302-20-9P 863302-21-0P
863302-22-1P 863302-23-2P 863302-24-3P
863302-25-4P 863302-26-5P 863302-27-6P
863302-28-7P 863302-29-8P 863302-30-1P
863302-31-2P 863302-32-3P 863302-33-4P
863302-34-5P 863302-35-6P 863302-36-7P
863302-37-8P 863302-38-9P 863302-39-0P
863302-40-3P 863302-41-4P 863302-42-5P
863302-43-6P 863302-44-7P 863302-45-8P
863302-46-9P 863302-47-0P 863302-48-1P
863302-49-2P 863302-50-5P 863302-51-6P
863302-52-7P 863302-53-8P 863302-54-9P
863302-55-0P 863302-56-1P 863302-57-2P
863302-58-3P 863302-59-4P 863302-60-7P
863302-61-8P 863302-62-9P 863302-63-0P

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
863302-64-1P 863302-65-2P 863302-66-3P
863302-67-4P 863302-68-5P 863302-69-6P
863302-70-9P 863302-71-0P 863302-72-1P
863302-73-2P 863302-74-3P 863302-75-4P
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863302-91-4P 863302-92-5P 863302-93-6P
863302-94-7P 863302-95-8P 863302-96-9P
863302-97-0P 863302-98-1P 863302-99-2P
863303-00-8P 863303-01-9P 863303-02-0P
863303-03-1P 863303-04-2P 863303-05-3P
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863303-76-8P 863303-77-9P 863303-78-0P
863303-79-1P 863303-80-4P 863303-81-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrrolidine compds. having bicyclic amide moiety as DPP-IV inhibitors for the treatment of diabetes)

RN 863302-11-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

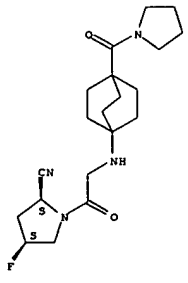
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-14-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-(1-pyrrolidinylcarbonyl)bicyclo[2.2.2]oct-1-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

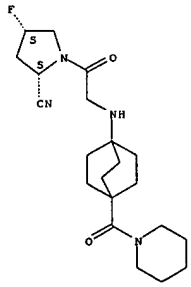
Absolute stereochemistry.



RN 863302-15-2 HCAPLUS
CN Piperidine, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]- (9CI) (CA INDEX NAME)

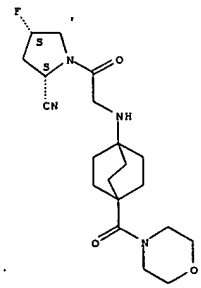
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-16-3 HCAPLUS
CN Morpholine, 4-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]- (9CI) (CA INDEX NAME)

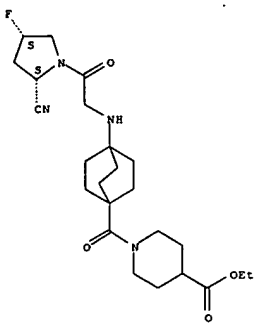
Absolute stereochemistry.



RN 863302-17-4 HCAPLUS
CN 4-Piperidinecarboxylic acid, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

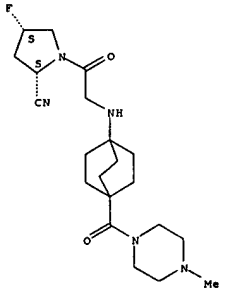
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-18-5 HCAPLUS
CN Piperazine, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

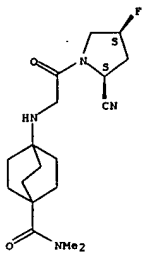
Absolute stereochemistry.



L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 863302-19-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

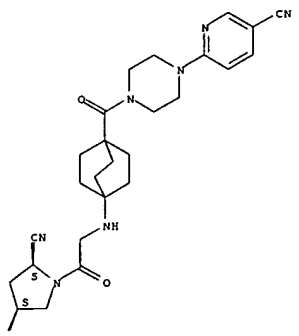


RN 863302-20-9 HCAPLUS
CN Piperazine, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-4-(5-cyano-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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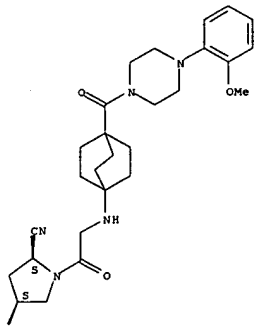


RN 863302-21-0 HCAPLUS
CN Piperazine, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-4-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A



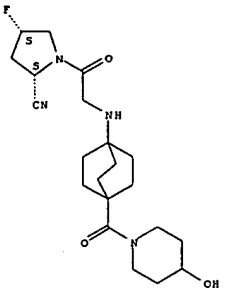
PAGE 2-A



RN 863302-22-1 HCAPLUS
CN 4-Piperidinol, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]- (9CI) (CA INDEX NAME)

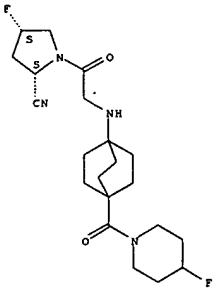
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-23-2 HCAPLUS
CN Piperidine, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-4-fluoro- (9CI) (CA INDEX NAME)

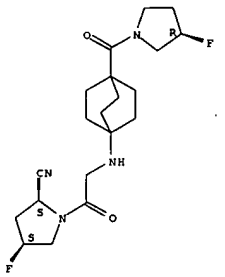
Absolute stereochemistry.



RN 863302-24-3 HCAPLUS

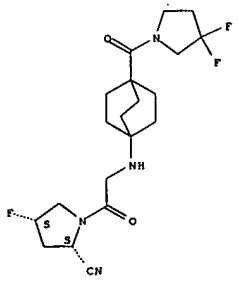
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 863302-26-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-[[(3R)-3-fluoro-1-pyrrolidinyl]carbonyl]bicyclo[2.2.2]oct-1-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 863302-27-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[4-[(3,3-difluoro-1-pyrrolidinyl)carbonyl]bicyclo[2.2.2]oct-1-yl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

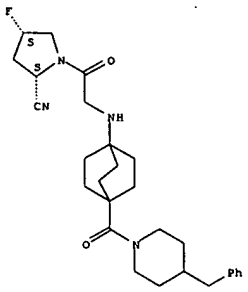
Absolute stereochemistry.



RN 863302-28-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-[[(3S)-3-fluoro-1-pyrrolidinyl]carbonyl]bicyclo[2.2.2]oct-1-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

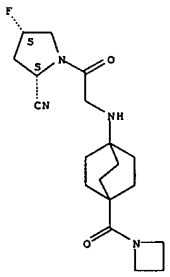
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Piperidine, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



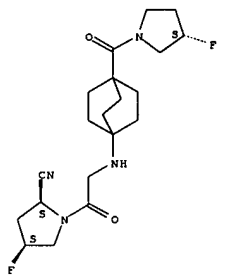
RN 863302-25-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[4-(1-azetidinylcarbonyl)bicyclo[2.2.2]oct-1-yl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



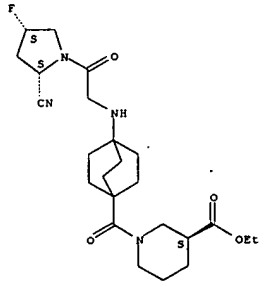
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.



RN 863302-29-8 HCAPLUS
CN 3-Piperidinecarboxylic acid, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-, ethyl ester, (3S)- (9CI) (CA INDEX NAME)

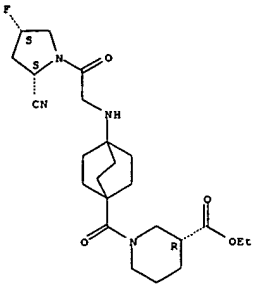
Absolute stereochemistry.



RN 863302-30-1 HCAPLUS
CN 3-Piperidinecarboxylic acid, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-, ethyl ester, (3R)- (9CI) (CA INDEX NAME)

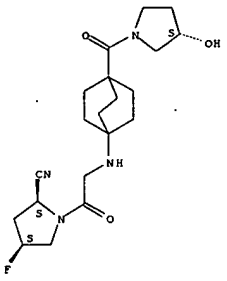
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-31-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-[[(3S)-3-hydroxy-1-pyrrolidinyl]carbonyl]bicyclo[2.2.2]oct-1-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

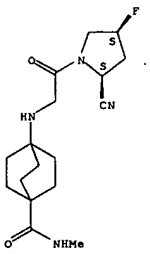


RN 863302-32-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-[[(3R)-3-hydroxy-1-pyrrolidinyl]carbonyl]bicyclo[2.2.2]oct-1-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

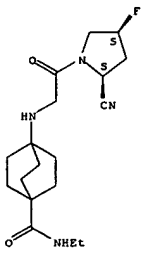
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.



RN 863302-35-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-ethyl- (9CI) (CA INDEX NAME)

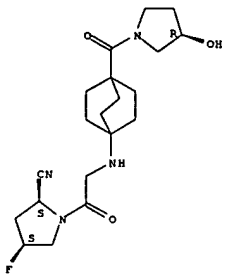
Absolute stereochemistry.



RN 863302-36-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-propyl- (9CI) (CA INDEX NAME)

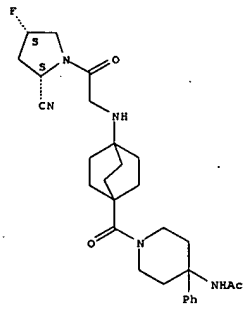
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



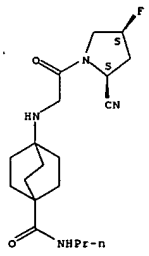
RN 863302-33-4 HCAPLUS
CN Acetamide, N-[1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-4-phenyl-4-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



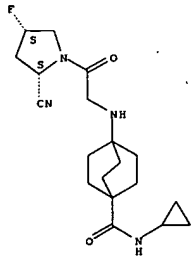
RN 863302-34-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-methyl- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-37-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-cyclopropyl- (9CI) (CA INDEX NAME)

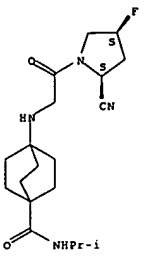
Absolute stereochemistry.



RN 863302-38-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

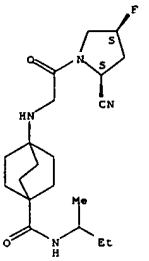
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-39-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(1-methylpropyl)- (9CI) (CA INDEX NAME)

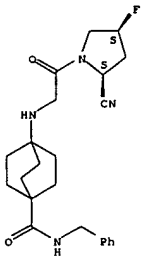
Absolute stereochemistry.



RN 863302-40-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

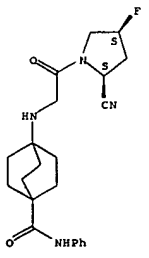
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-43-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-phenyl- (9CI) (CA INDEX NAME)

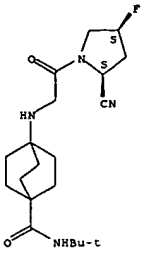
Absolute stereochemistry.



RN 863302-44-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)- (9CI) (CA INDEX NAME)

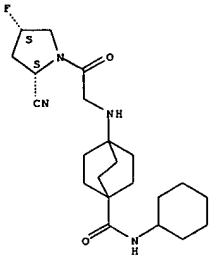
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-41-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-cyclohexyl- (9CI) (CA INDEX NAME)

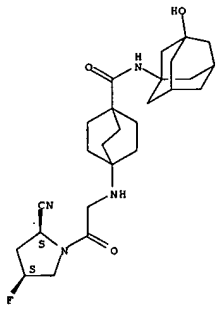
Absolute stereochemistry.



RN 863302-42-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

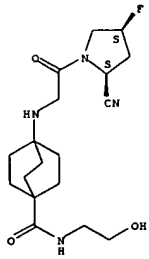
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-45-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

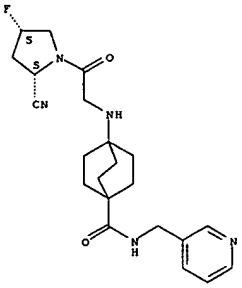
Absolute stereochemistry.



RN 863302-46-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)

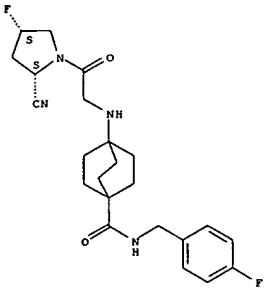
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



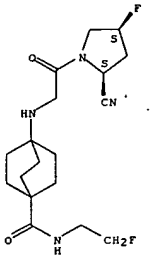
RN 863302-47-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



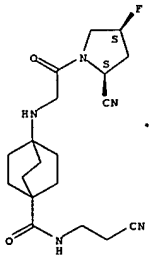
RN 863302-48-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(diphenylmethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-51-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-(2-cyanoethyl)-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

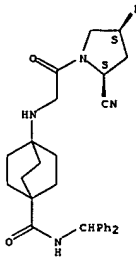


RN 863302-52-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-butyl-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

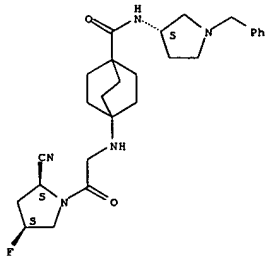
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.



RN 863302-49-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(3S)-1-(phenylmethyl)-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

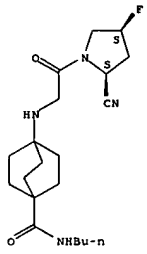
Absolute stereochemistry.



RN 863302-50-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(2-fluoroethyl)- (9CI) (CA INDEX NAME)

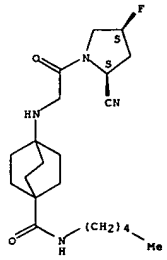
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-53-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-pentyl- (9CI) (CA INDEX NAME)

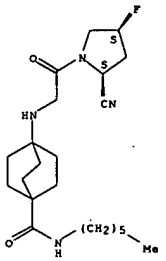
Absolute stereochemistry.



RN 863302-54-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-hexyl- (9CI) (CA INDEX NAME)

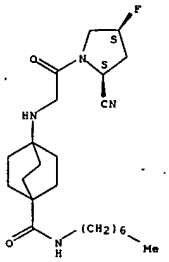
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-55-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-heptyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

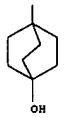


RN 863302-56-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-octyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

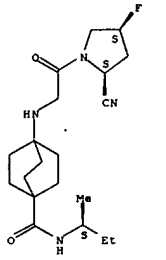
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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RN 863302-58-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1S)-1-methylpropyl]- (9CI) (CA INDEX NAME)

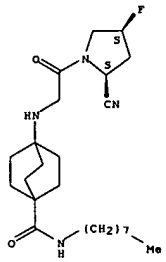
Absolute stereochemistry.



RN 863302-59-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1R)-1-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

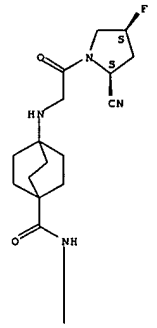
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



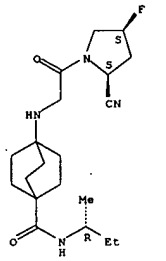
RN 863302-57-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-hydroxybicyclo[2.2.2]oct-1-yl)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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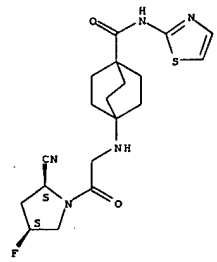


L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-60-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-2-thiazolyl- (9CI) (CA INDEX NAME)

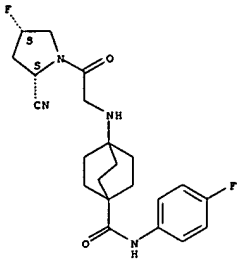
Absolute stereochemistry.



RN 863302-61-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-fluorophenyl)- (9CI) (CA INDEX NAME)

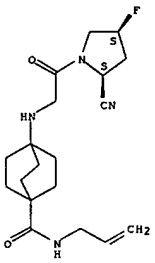
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-62-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-2-propenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



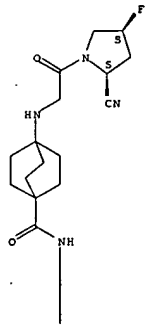
RN 863302-63-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(3S)-hexahydro-2-oxo-1H-azepin-3-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

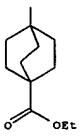
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.

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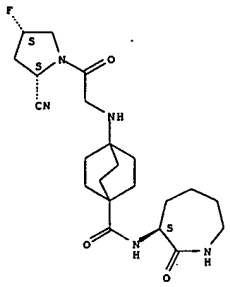
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RN 863302-66-3 HCAPLUS
CN 1,4'-Bipiperidine, 1'-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]- (9CI) (CA INDEX NAME)

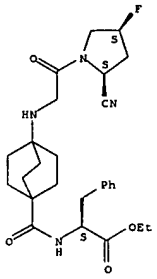
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-64-1 HCAPLUS .
CN L-Phenylalanine, N-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

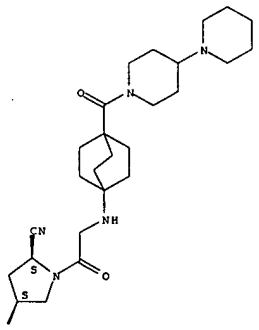
Absolute stereochemistry.



RN 863302-65-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid, 4-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

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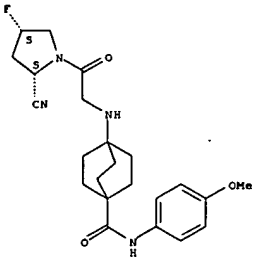
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RN 863302-67-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

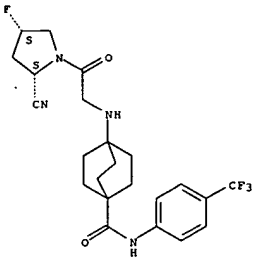
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-68-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

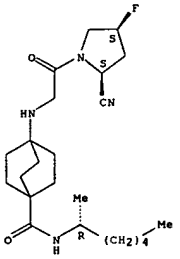
Absolute stereochemistry.



RN 863302-69-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-tricyclo[3.3.1.13,7]dec-1-yl- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

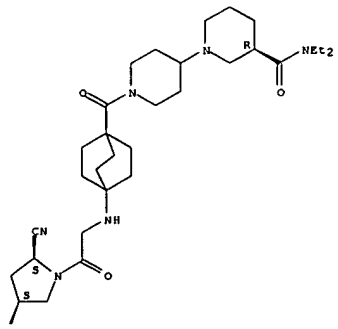
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



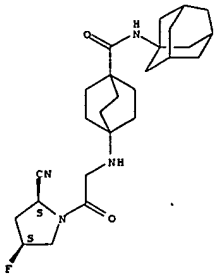
RN 863302-72-1 HCAPLUS
CN [1,4'-Bipiperidine]-3-carboxamide, 1'-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-N,N-diethyl-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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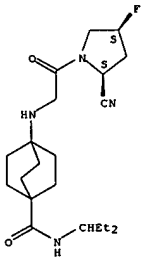


L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-70-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(1-ethylpropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 863302-71-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1R)-1-methylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

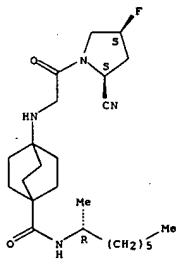
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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RN 863302-73-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1R)-1-methylheptyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

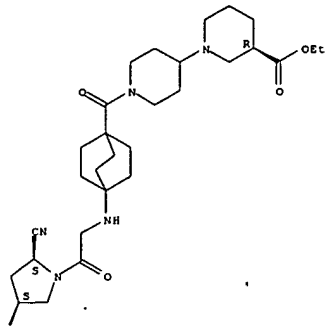


RN 863302-74-3 HCAPLUS
CN [1,4'-Bipiperidine]-3-carboxylic acid, 1'-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]-, ethyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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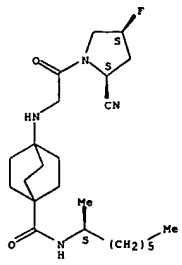
PAGE 2-A



RN 863302-75-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1S)-1-methylheptyl]- (9CI) (CA INDEX NAME)

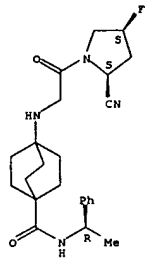
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-76-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1R)-1-phenylethyl]- (9CI) (CA INDEX NAME)

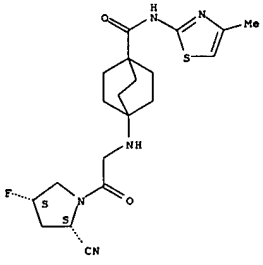
Absolute stereochemistry.



RN 863302-77-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-methyl-2-thiazolyl)- (9CI) (CA INDEX NAME)

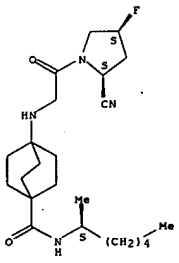
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-78-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1S)-1-methylhexyl]- (9CI) (CA INDEX NAME)

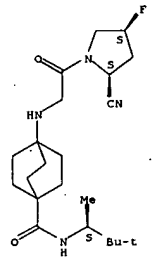
Absolute stereochemistry.



RN 863302-79-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1S)-1,2,2-trimethylpropyl]- (9CI) (CA INDEX NAME)

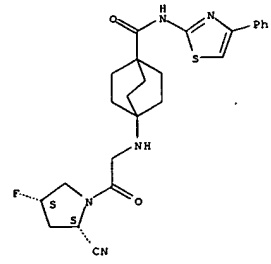
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-80-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-phenyl-2-thiazolyl)- (9CI) (CA INDEX NAME)

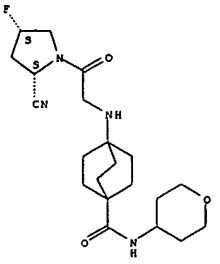
Absolute stereochemistry.



RN 863302-81-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(tetrahydro-2H-pyran-4-yl)- (9CI) (CA INDEX NAME)

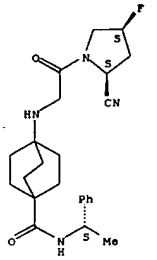
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-82-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1S)-1-phenylethyl]- (9CI) (CA INDEX NAME)

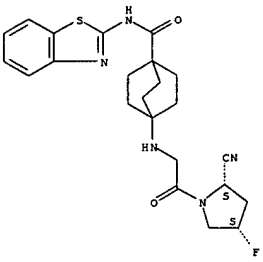
Absolute stereochemistry.



RN 863302-83-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-(4-chlorophenyl)-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

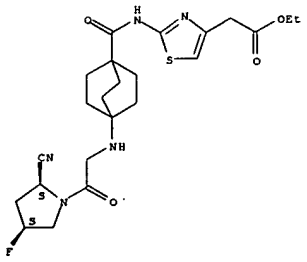
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-86-7 HCAPLUS
CN 4-Thiazoleacetic acid, 2-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

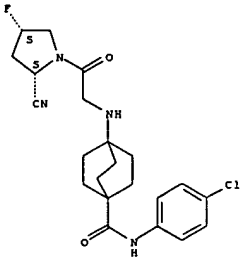
Absolute stereochemistry.



RN 863302-87-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-methylphenyl)- (9CI) (CA INDEX NAME)

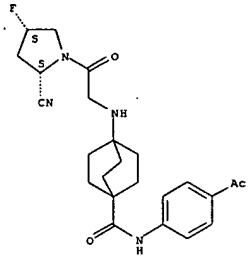
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-84-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-(4-acetylphenyl)-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

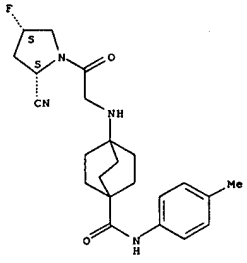
Absolute stereochemistry.



RN 863302-85-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-2-benzothiazolyl-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

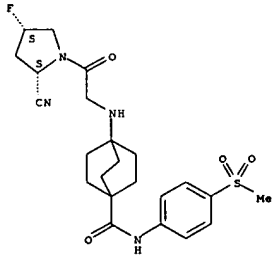
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-88-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

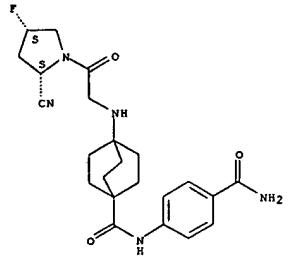
Absolute stereochemistry.



RN 863302-89-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-[4-(aminocarbonyl)phenyl]-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

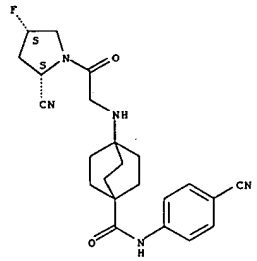
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-90-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-cyanophenyl)- (9CI) (CA INDEX NAME)

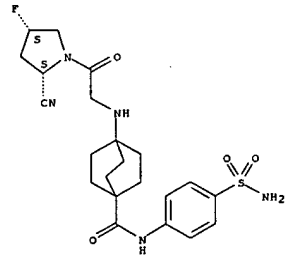
Absolute stereochemistry.



RN 863302-91-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-[(trifluoromethyl)sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

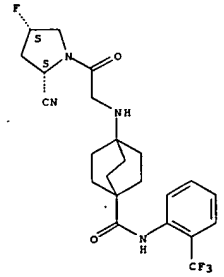
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-94-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

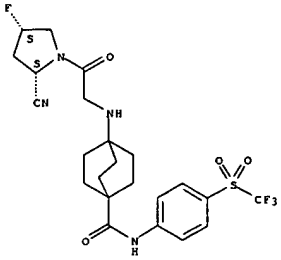
Absolute stereochemistry.



RN 863302-95-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(2-fluorophenyl)- (9CI) (CA INDEX NAME)

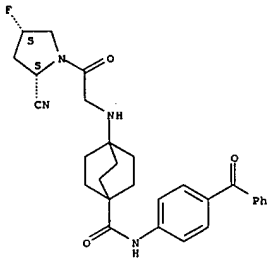
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-92-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-(4-benzoylphenyl)-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

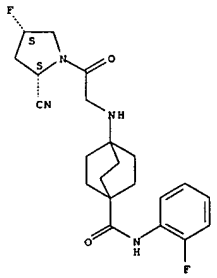
Absolute stereochemistry.



RN 863302-93-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-[4-(aminosulfonyl)phenyl]-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

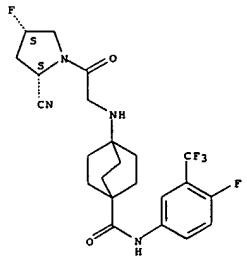
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-96-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-fluoro-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

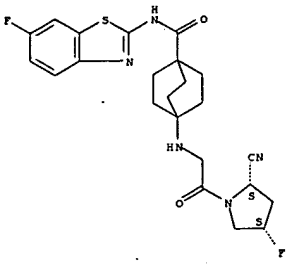
Absolute stereochemistry.



RN 863302-97-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(6-fluoro-2-benzothiazolyl)- (9CI) (CA INDEX NAME)

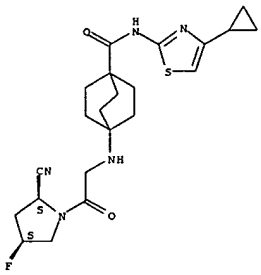
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863302-98-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-cyclopropyl-2-thiazolyl)- (9CI) (CA INDEX NAME)

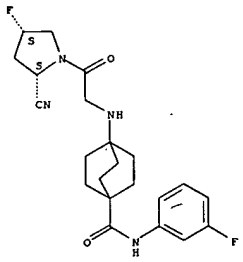
Absolute stereochemistry.



RN 863302-99-2 HCAPLUS
CN 5-Thiazolecarboxylic acid, 2-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]-4-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

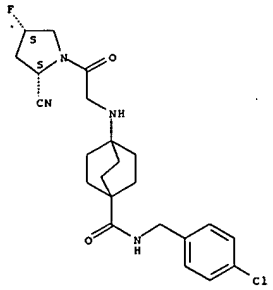
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-02-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-[(4-chlorophenyl)methyl]-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

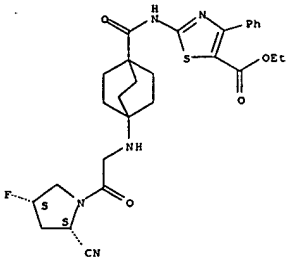
Absolute stereochemistry.



RN 863303-03-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-fluoro-2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

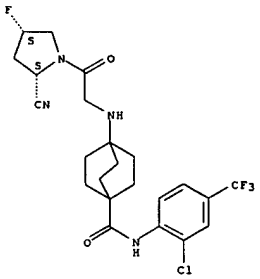
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-00-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-[2-chloro-4-(trifluoromethyl)phenyl]-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

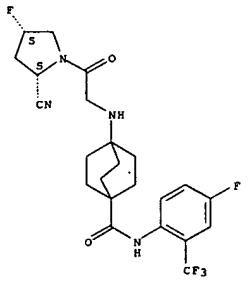
Absolute stereochemistry.



RN 863303-01-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(3-fluorophenyl)- (9CI) (CA INDEX NAME)

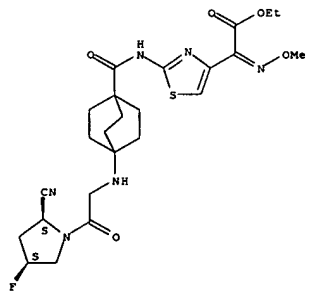
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-04-2 HCAPLUS
CN 4-Thiazoleacetic acid, 2-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]-α-(methoxyimino)-, ethyl ester (9CI) (CA INDEX NAME)

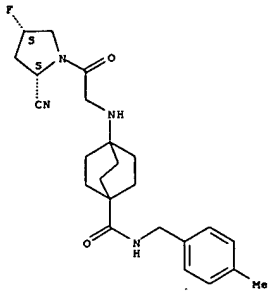
Absolute stereochemistry.
Double bond geometry unknown.



RN 863303-05-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

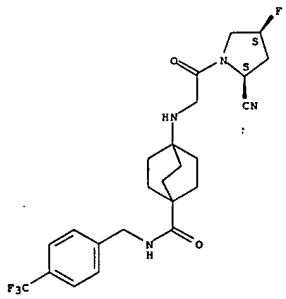
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



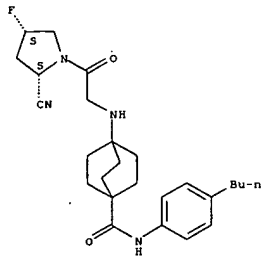
RN 863303-06-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



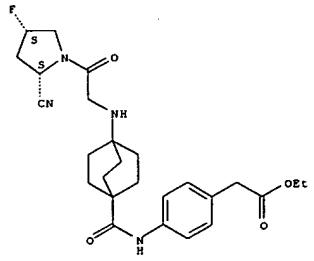
RN 863303-07-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



RN 863303-10-0 HCAPLUS
CN Benzeneacetic acid, 4-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

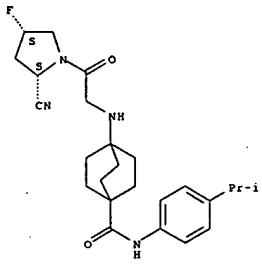


RN 863303-11-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

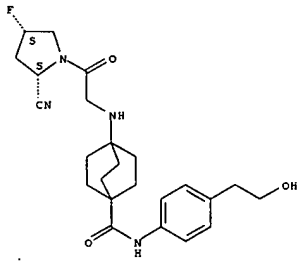
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(1-methylethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



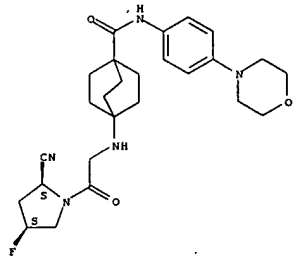
RN 863303-08-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(2-hydroxyethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



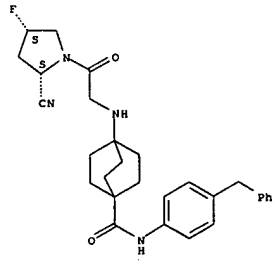
RN 863303-09-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-(4-butylphenyl)-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-12-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(phenylmethyl)phenyl]- (9CI) (CA INDEX NAME)

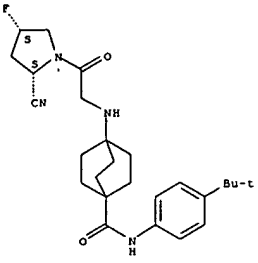
Absolute stereochemistry.



RN 863303-13-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(1,1-dimethylethyl)phenyl]- (9CI) (CA INDEX NAME)

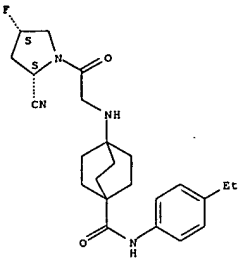
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-14-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-ethylphenyl)- (9CI) (CA INDEX NAME)

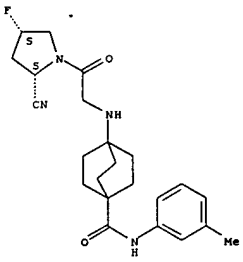
Absolute stereochemistry.



RN 863303-15-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-(3-chlorophenyl)-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

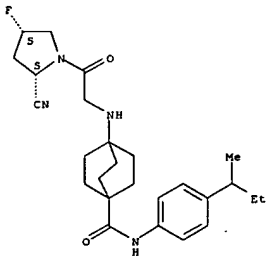
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-18-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(1-methylpropyl)phenyl]- (9CI) (CA INDEX NAME)

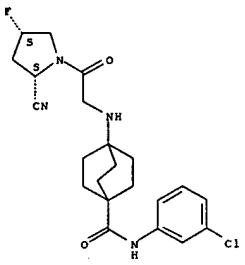
Absolute stereochemistry.



RN 863303-19-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-octylphenyl)- (9CI) (CA INDEX NAME)

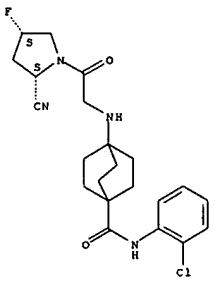
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-16-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-(2-chlorophenyl)-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

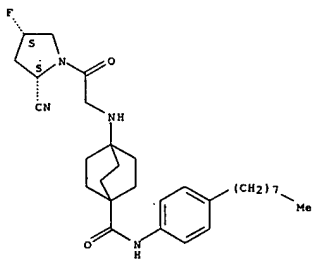
Absolute stereochemistry.



RN 863303-17-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(3-methylphenyl)- (9CI) (CA INDEX NAME)

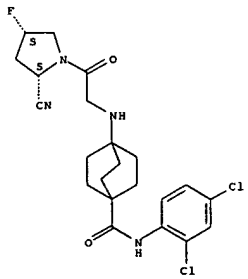
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-20-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(2,4-dichlorophenyl)- (9CI) (CA INDEX NAME)

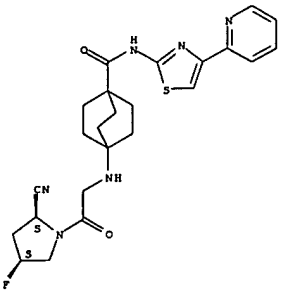
Absolute stereochemistry.



RN 863303-21-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(2-pyridinyl)-2-thiazolyl]- (9CI) (CA INDEX NAME)

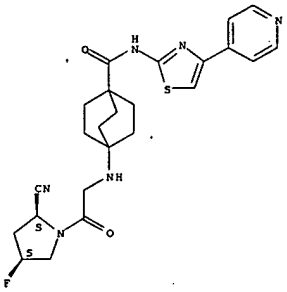
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-22-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(4-pyridinyl)-2-thiazolyl]- (9CI) (CA INDEX NAME)

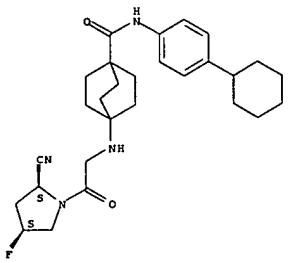
Absolute stereochemistry.



RN 863303-23-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(2-methylphenyl)- (9CI) (CA INDEX NAME)

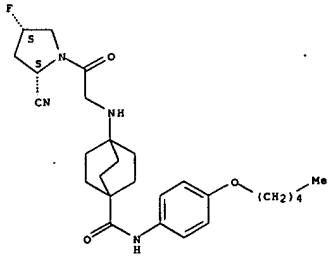
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
pyrrolidinyl]-2-oxoethyl]amino]-N-(4-cyclohexylphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 863303-26-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(pentyloxy)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

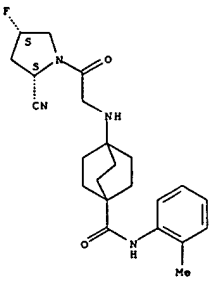


RN 863303-27-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(2-phenylethenyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

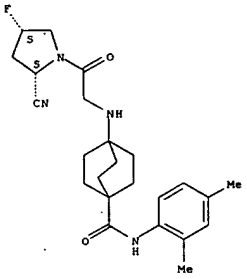
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.



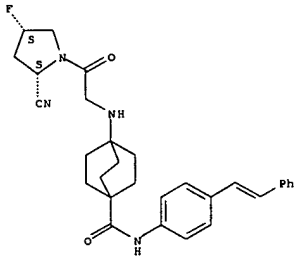
RN 863303-24-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(2,4-dimethylphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



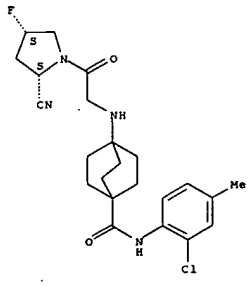
RN 863303-25-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-28-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-(2-chloro-4-methylphenyl)-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

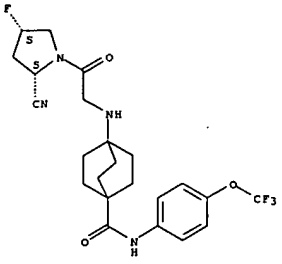
Absolute stereochemistry.



RN 863303-29-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)

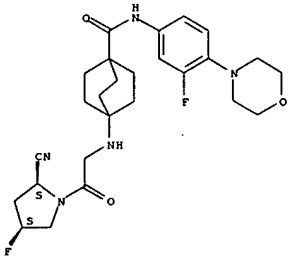
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-30-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[3-fluoro-4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)

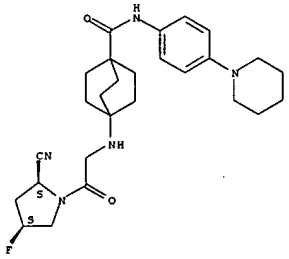
Absolute stereochemistry.



RN 863303-31-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-ethynylphenyl)- (9CI) (CA INDEX NAME)

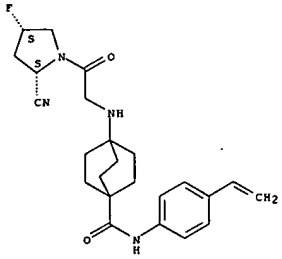
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-34-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-ethenylphenyl)- (9CI) (CA INDEX NAME)

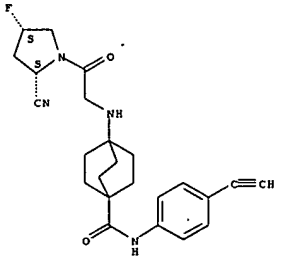
Absolute stereochemistry.



RN 863303-35-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(2,4,6-trimethylphenyl)- (9CI) (CA INDEX NAME)

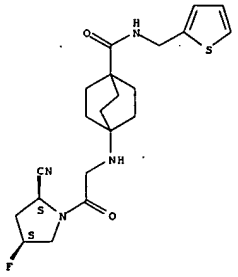
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-32-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(2-thienylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

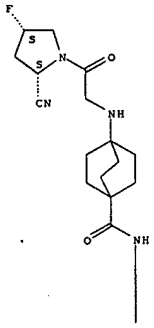


RN 863303-33-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(1-piperidinyl)phenyl]- (9CI) (CA INDEX NAME)

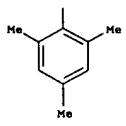
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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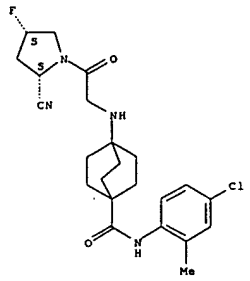
PAGE 2-A



RN 863303-36-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-(4-chloro-2-methylphenyl)-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

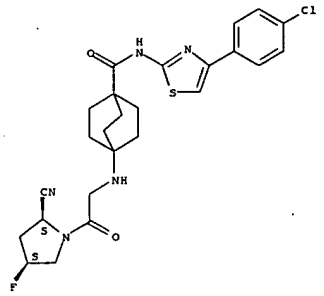
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



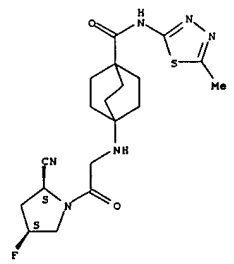
RN 863303-37-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-[4-(4-chlorophenyl)-2-thiazolyl]-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



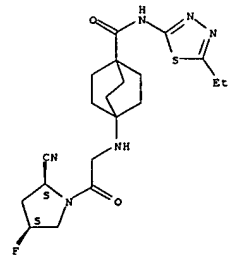
RN 863303-38-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-1,3,4-thiadiazol-2-yl- (9CI) (CA INDEX

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



RN 863303-41-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(5-ethyl-1,3,4-thiadiazol-2-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

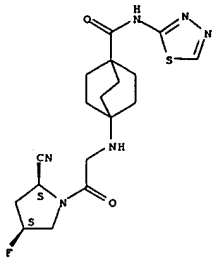


RN 863303-42-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4,4-difluorocyclohexyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

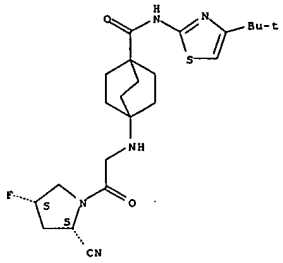
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
NAME)

Absolute stereochemistry.



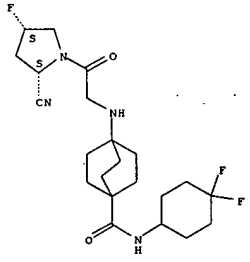
RN 863303-39-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(1,1-dimethylethyl)-2-thiazolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



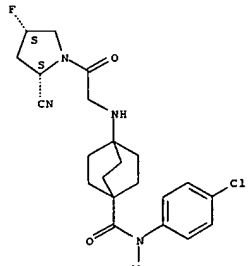
RN 863303-40-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(5-methyl-1,3,4-thiadiazol-2-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-43-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-(4-chlorophenyl)-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-methyl- (9CI) (CA INDEX NAME)

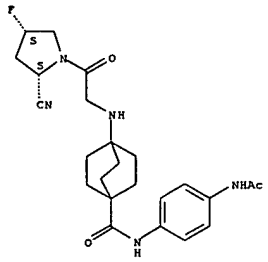
Absolute stereochemistry.



RN 863303-44-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-[4-(acetylamino)phenyl]-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

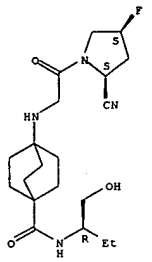
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-45-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1R)-1-(hydroxymethyl)propyl]- (9CI) (CA INDEX NAME)

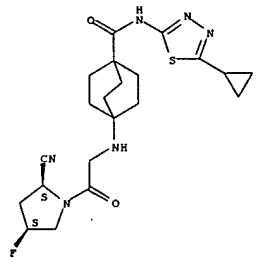
Absolute stereochemistry.



RN 863303-46-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]- (9CI) (CA INDEX NAME)

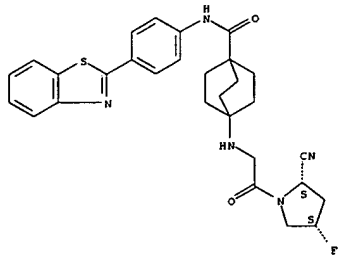
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-49-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-[4-(2-benzothiazolyl)phenyl]-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

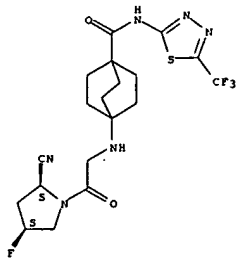
Absolute stereochemistry.



RN 863303-50-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(1-pyrrolidinyl)phenyl]- (9CI) (CA INDEX NAME)

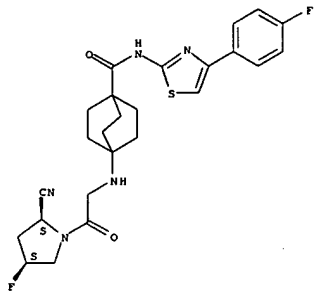
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-47-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[4-(4-fluorophenyl)-2-thiazolyl]- (9CI) (CA INDEX NAME)

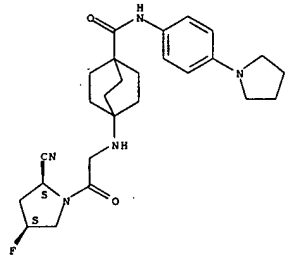
Absolute stereochemistry.



RN 863303-48-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(5-cyclopropyl-1,3,4-thiadiazol-2-yl)- (9CI) (CA INDEX NAME)

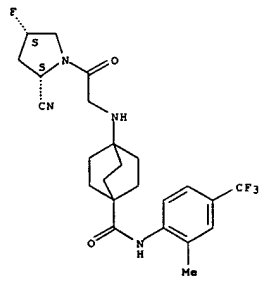
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-51-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[2-methyl-4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

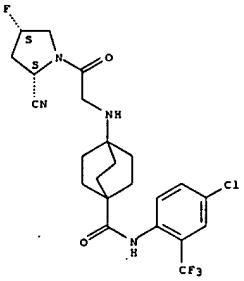
Absolute stereochemistry.



RN 863303-52-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N-[4-chloro-2-(trifluoromethyl)phenyl]-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

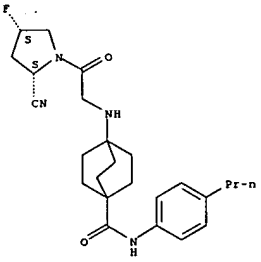
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-53-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-propylphenyl)- (9CI) (CA INDEX NAME)

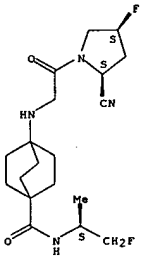
Absolute stereochemistry.



RN 863303-54-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-pentylphenyl)- (9CI) (CA INDEX NAME)

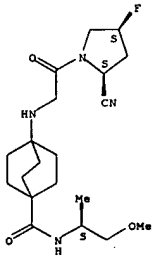
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-57-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1S)-2-methoxy-1-methylethyl]- (9CI) (CA INDEX NAME)

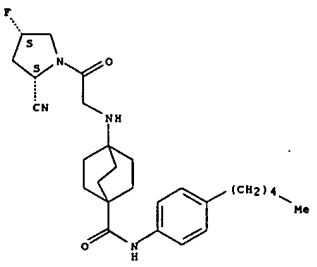
Absolute stereochemistry.



RN 863303-58-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(5-tricyclo[3.3.1.13,7]dec-1-yl-1,3,4-thiadiazol-2-yl)- (9CI) (CA INDEX NAME)

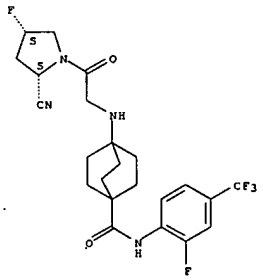
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-55-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[2-fluoro-4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

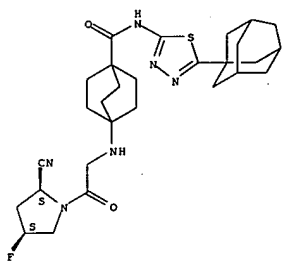
Absolute stereochemistry.



RN 863303-56-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1S)-2-fluoro-1-methylethyl]- (9CI) (CA INDEX NAME)

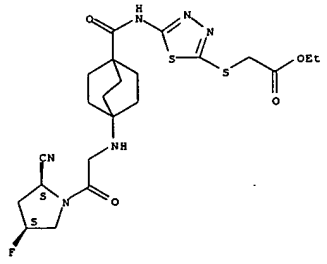
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-59-7 HCAPLUS
CN Acetic acid, [[5-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]-1,3,4-thiadiazol-2-yl]thio]-, ethyl ester (9CI) (CA INDEX NAME)

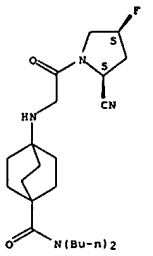
Absolute stereochemistry.



RN 863303-60-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, N,N-dibutyl-4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

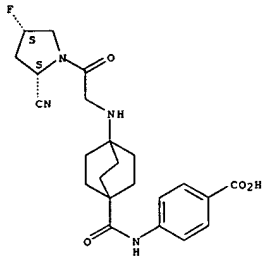
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-62-2 HCAPLUS
CN Benzoic acid, 4-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)

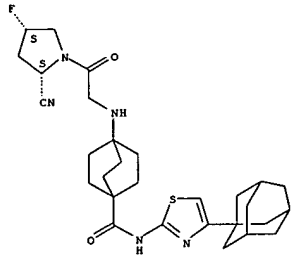
Absolute stereochemistry.



RN 863303-63-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1R)-2-fluoro-1-methylethyl]- (9CI) (CA INDEX NAME)

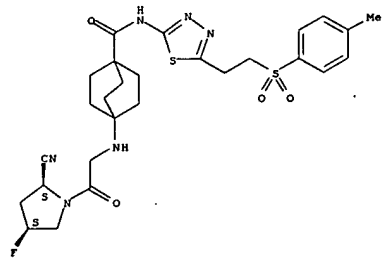
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-66-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[5-[2-[(4-methylphenyl)sulfonyl]ethyl]-1,3,4-thiadiazol-2-yl]- (9CI) (CA INDEX NAME)

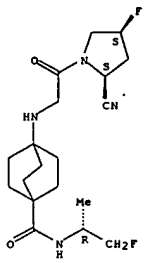
Absolute stereochemistry.



RN 863303-67-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(5-methyl-1,3,4-oxadiazol-2-yl)- (9CI) (CA INDEX NAME)

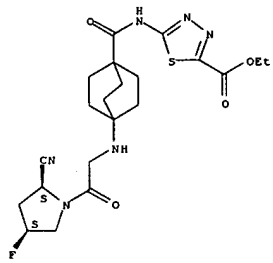
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-64-4 HCAPLUS
CN 1,3,4-Thiadiazole-2-carboxylic acid, 5-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

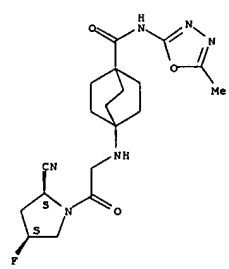
Absolute stereochemistry.



RN 863303-65-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(4-tricyclo[3.3.1.13,7]dec-1-yl-2-thiazolyl)- (9CI) (CA INDEX NAME)

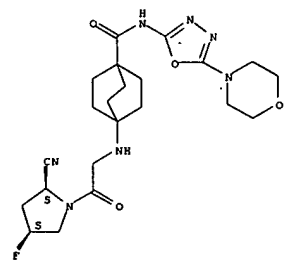
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-68-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[5-(4-morpholinyl)-1,3,4-oxadiazol-2-yl]- (9CI) (CA INDEX NAME)

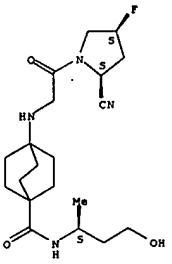
Absolute stereochemistry.



RN 863303-69-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1S)-3-hydroxy-1-methylpropyl]- (9CI) (CA INDEX NAME)

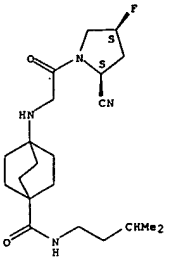
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-70-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(3-methylbutyl)- (9CI) (CA INDEX NAME)

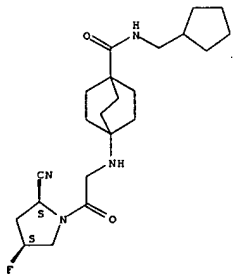
Absolute stereochemistry.



RN 863303-71-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(3,3-dimethylbutyl)- (9CI) (CA INDEX NAME)

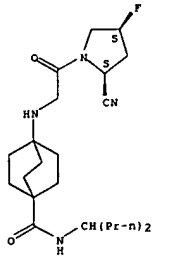
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-74-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(1-propylbutyl)- (9CI) (CA INDEX NAME)

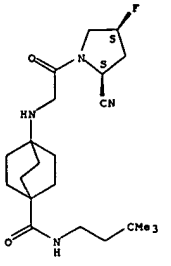
Absolute stereochemistry.



RN 863303-75-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1R,2S)-2-fluorocyclopropyl]- (9CI) (CA INDEX NAME)

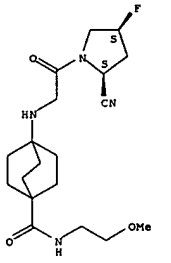
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-72-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(2-methoxyethyl)- (9CI) (CA INDEX NAME)

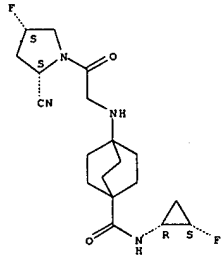
Absolute stereochemistry.



RN 863303-73-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(cyclopentylmethyl)- (9CI) (CA INDEX NAME)

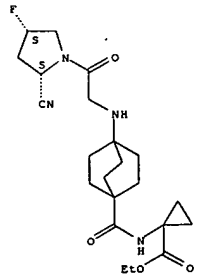
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 863303-76-8 HCAPLUS
CN Cyclopropanecarboxylic acid, 1-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

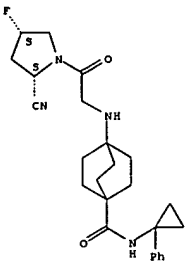
Absolute stereochemistry.



RN 863303-77-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(1-phenylcyclopropyl)- (9CI) (CA INDEX NAME)

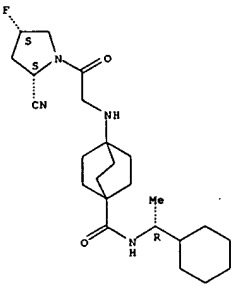
Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



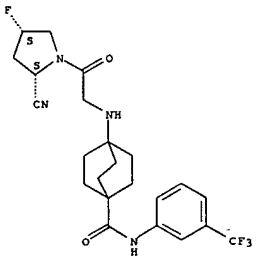
RN 863303-78-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[(1R)-1-cyclohexylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



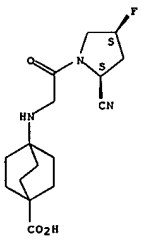
RN 863303-79-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(5-methyl-2-thiazolyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 862501-98-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrrolidine compds. having bicyclic amide moiety as DPP-IV inhibitors for the treatment of diabetes)
RN 862501-98-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

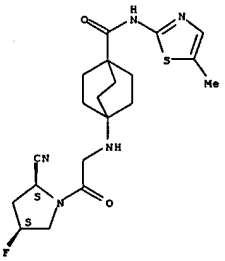
Absolute stereochemistry.



IT 862501-64-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrolidine compds. having bicyclic amide moiety as DPP-IV inhibitors for the treatment of diabetes)
RN 862501-64-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-

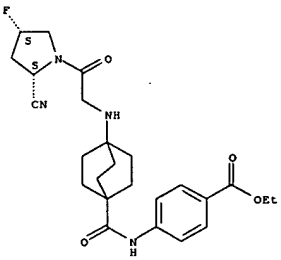
L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.



RN 863303-80-4 HCAPLUS
CN Benzoic acid, 4-[[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]bicyclo[2.2.2]oct-1-yl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

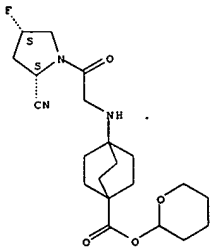


RN 863303-81-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
pyrrolidinyl]-2-oxoethyl]amino]-, tetrahydro-2H-pyran-2-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

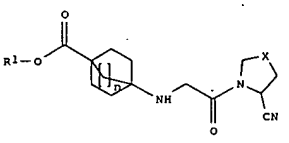


REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 18 Aug 2005
ACCESSION NUMBER: 2005:811738 HCAPLUS
DOCUMENT NUMBER: 143:211834
TITLE: Preparation of pyrrolidine compounds having bicyclic moiety as DPP-IV inhibitors
INVENTOR(S): Fukuda, Yasumichi; Asahina, Yoshikazu; Ohata, Kohei; Yokota, Kazuya; Murakami, Koji; Matsui, Toshiyuki
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075421	A1	20050818	WO 2005-JP1377	20050201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005210285	A1	20050818	AU 2005-210285	20050201
CA 2554493	A1	20050818	CA 2005-2554493	20050201
EP 1712547	A1	20061018	EP 2005-704327	20050201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
NO 2006003486	A	20060829	NO 2006-3486	20060731
PRIORITY APPLN. INFO.:			JP 2004-29856 A	20040205
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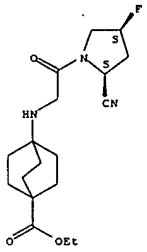
OTHER SOURCE(S): MARPAT 143:211834
GI



I

L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
AB Title compds. I [R1 = (un)substituted alkyl, etc.; X = CH2, etc.; n = 1-3] were prepared For example, treatment of 4-aminobicyclo[2.2.2]octane-1-carboxylic acid Et ester, e.g., prepared from bicyclo[2.2.2]octane-1,4-dicarboxylic acid monomethyl ester in 4 steps, with (2S,4S)-1-(2-bromoacetyl)-4-fluoropyrrolidine-2-carbonitrile afforded (2S,4S)-1-[[N-(4-ethoxycarbonylbicyclo[2.2.2]oct-1-yl]amino]acetyl]-4-fluoropyrrolidine-2-carbonitrile (II). In DPP-IV (dipeptidylpeptidase IV) inhibition assays, the IC50 value of compound II was 0.25 nmol/mL. Compds. I are claimed useful for the treatment of diabetes.
IT 862501-61-9P 862501-64-2P 862501-66-4P
862501-68-6P 862501-69-7P 862501-70-0P
862501-71-1P 862501-74-4P 862501-76-6P
862501-78-8P 862501-79-9P 862501-81-3P
862501-83-5P 862501-84-6P 862501-85-7P
862501-86-8P 862501-87-9P 862501-88-0P
862501-89-1P 862501-90-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidine compds. as DPP-IV inhibitors for treatment of diabetes)
RN 862501-61-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

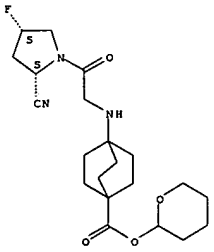
Absolute stereochemistry.



RN 862501-64-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-, tetrahydro-2H-pyran-2-yl ester (9CI)

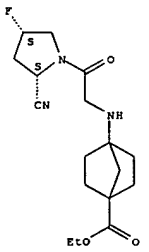
L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry.



RN 862501-66-4 HCAPLUS
CN Bicyclo[2.2.1]heptane-1-carboxylic acid, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

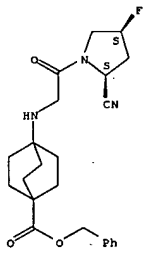
Absolute stereochemistry.



RN 862501-68-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)

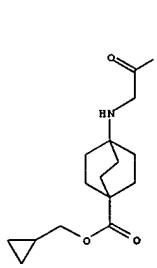
Absolute stereochemistry.

L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 862501-69-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-, cyclopropylmethyl ester (9CI) (CA INDEX NAME)

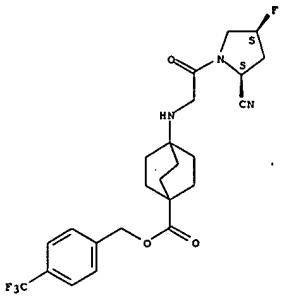
Absolute stereochemistry.



RN 862501-70-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-, [4-(trifluoromethyl)phenyl]methyl ester (9CI) (CA INDEX NAME)

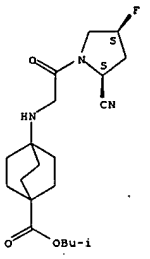
Absolute stereochemistry.

L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 862501-71-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

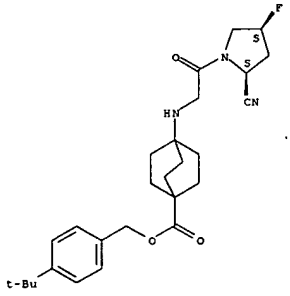


RN 862501-74-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, 1-methylethyl ester (9CI) (CA INDEX

L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862501-78-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, [4-(1,1-dimethylethyl)phenyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

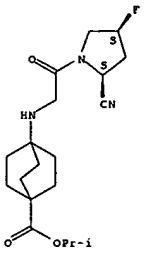


RN 862501-79-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, (4-chlorophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

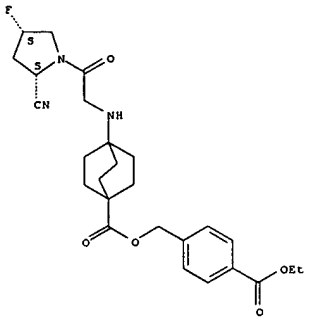
L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
NAME)

Absolute stereochemistry.

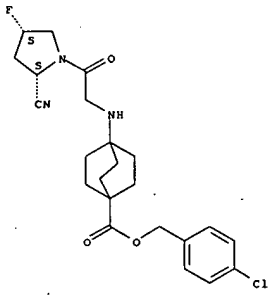


RN 862501-76-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, [4-(ethoxycarbonyl)phenyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

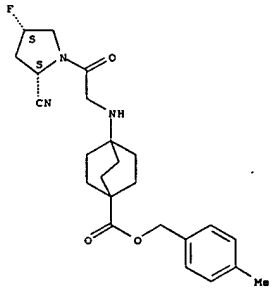


L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 862501-81-3 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, (4-methylphenyl)methyl ester (9CI) (CA INDEX NAME)

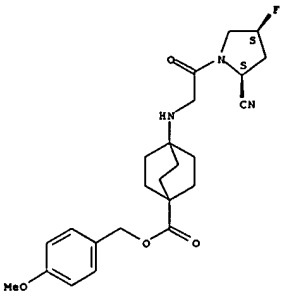
Absolute stereochemistry.



RN 862501-83-5 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, (4-methoxyphenyl)methyl ester (9CI) (CA

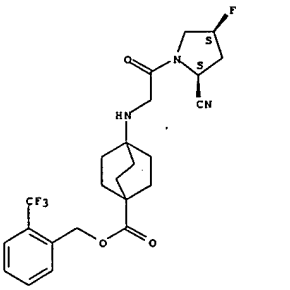
L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.

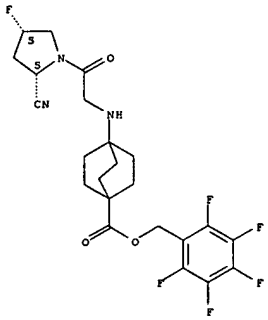


RN 862501-84-6 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, [2-(trifluoromethyl)phenyl]methyl ester
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

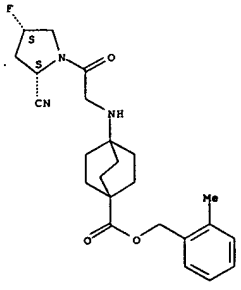


L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 862501-87-9 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, (2-methylphenyl)methyl ester (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

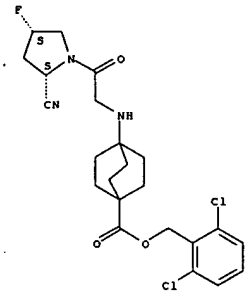


RN 862501-88-0 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, (1S)-1-phenylethyl ester (9CI) (CA

L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862501-85-7 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, (2,6-dichlorophenyl)methyl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

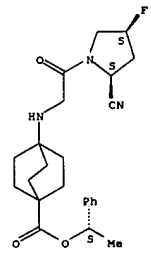


RN 862501-86-8 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, (pentafluorophenyl)methyl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

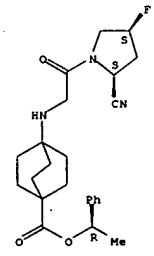
L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.



RN 862501-89-1 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, (1R)-1-phenylethyl ester (9CI) (CA
INDEX NAME)

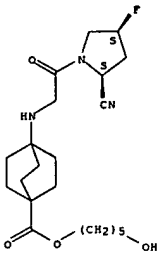
Absolute stereochemistry.



RN 862501-90-4 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid,
4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-
pyrrolidinyl]-2-oxoethyl]amino]-, 5-hydroxypentyl ester (9CI) (CA INDEX
NAME)

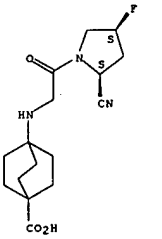
Absolute stereochemistry.

L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 862501-98-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrrolidine compds. as DPP-IV inhibitors for treatment of
diabetes)
RN 862501-98-2 HCAPLUS
CN Bicyclo[2.2.2]octane-1-carboxylic acid, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

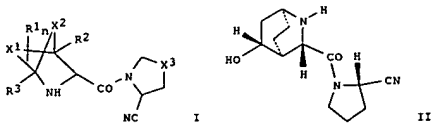


REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 24 Jun 2005
ACCESSION NUMBER: 2005:547270 HCAPLUS
DOCUMENT NUMBER: 143:78074
TITLE: Preparation of azabicycle-containing 2-cyanopyrrolidinecarboxamides as dipeptidyl peptidase-IV inhibitors useful for treating non-insulin-dependent diabetes mellitus
INVENTOR(S): Shima, Ichiro; Kuroda, Akio; Ohkawa, Takehiko; Kurosaki, Toshio; Sawada, Yuki; Wada, Aiko
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005137224	A1	20050623	US 2004-975524		20041029
PRIORITY APPLN. INFO.:			EP 2003-906010	A	20031031
			EP 2004-900961	A	20040225

OTHER SOURCE(S): MARPAT 143:78074
GI



I II

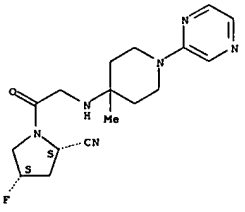
AB 2-Cyanopyrrolidinecarboxamides I [X1 and X2 = alkylene; X3 = CH2, CHF or CF2; R1 = OR4, NR5R6, :NR7; R2-3 = H, alkyl; n = 0-4] are prepared, e.g., II, have activity inhibiting DPP-IV. For example, (2S)-1-[[(1S,3S,4S,5S,6R)-5,6-dihydroxy-2-azabicyclo[2.2.2]oct-3-yl]carbonyl]-2-pyrrolidinecarbonitrile hydrochloride was prepared in 5 steps starting from Et (1S,3S,4R)-2-((1R)-1-phenylethyl)-2-azabicyclo[2.2.2]oct-5-ene-3-carboxylate and involving intermediates Et (1S,3S,4S,5S,6R)-5,6-dihydroxy-2-((1R)-1-phenylethyl)-2-azabicyclo[2.2.2]octane-3-carboxylate, Et (1S,3S,4S,5S,6R)-5,6-dihydroxy-2-azabicyclo[2.2.2]octane-3-carboxylate, (1S,3S,4S,5S,6R)-2-(tert-Butoxycarbonyl)-5,6-dihydroxy-2-azabicyclo[2.2.2]octane-3-carboxylic acid and tert-Bu (1S,3S,4S,5S,6R)-3-[[(2S)-2-cyano-1-pyrrolidinyl]carbonyl]-5,6-dihydroxy-2-azabicyclo[2.2.2]octane-2-carboxylate. I are useful in the treatment of conditions mediated by DPP-IV, such as NIDDM. IC50 values for inhibiting DPP-IV are tabulated for 6 claimed compds. (e.g. 8.5 nM for II). A method

L4 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L4 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
of prepn. is claimed (deprotection of N-protected I) and 46 example prepns. are included.

IT 851389-46-3P, (2S,4S)-4-Fluoro-1-[[[4-methyl-1-(2-pyrazinyl)-4-piperidinyl]amino]acetyl]-2-pyrrolidinecarbonitrile 851390-47-1P, (2S,4S)-4-Fluoro-1-[[[1-methyl-1,2,3,4-tetrahydro-4-quinolinyl]amino]acetyl]-2-pyrrolidinecarbonitrile 851455-62-4P, (2S,4S)-4-Fluoro-1-[[[(1R,5S)-3-methyl-8-(2-pyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-2-pyrrolidinecarbonitrile
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of azabicycle-containing 2-cyanopyrrolidinecarboxamides as dipeptidyl peptidase-IV inhibitors useful for treating non-insulin-dependent diabetes mellitus)
RN 851389-46-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(4-methyl-1-pyrazinyl-4-piperidinyl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

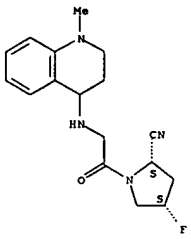
Absolute stereochemistry.



RN 851390-47-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(1,2,3,4-tetrahydro-1-methyl-4-quinolinyl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

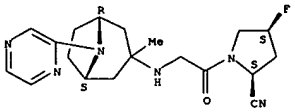
Absolute stereochemistry.

L4 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 851455-62-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(1R,5S)-3-methyl-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



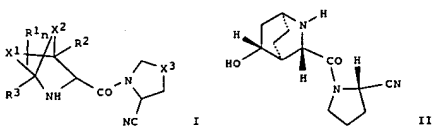
L4 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 13 May 2005
ACCESSION NUMBER: 2005:409520 HCAPLUS
DOCUMENT NUMBER: 142:463593
TITLE: Preparation of azabicycle-containing 2-cyanopyrrolidinecarboxamides as dipeptidyl peptidase-IV inhibitors useful for treating non-insulin-dependent diabetes mellitus
INVENTOR(S): Shima, Ichiro; Kuroda, Akio; Ohkawa, Takehiko; Kurosaki, Toshio; Sawada, Yuki; Wada, Aiko
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042533	A2	20050512	WO 2004-JP16469	20041029
WO 2005042533	A3	20050901		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004285809	A1	20050512	AU 2004-285809	20041029
CA 2543533	A1	20050512	CA 2004-2543533	20041029
CN 1871237	A	20061129	CN 2004-80031557	20041029
EP 1737863	A2	20070103	EP 2004-793389	20041029
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
NO 2006002517	A	20060721	NO 2006-2517	20060531

PRIORITY APPLN. INFO.: AU 2003-906010 A 20031031
AU 2004-900961 A 20040225
WO 2004-JP16469 W 20041029

OTHER SOURCE(S): MARPAT 142:463593
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L4 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



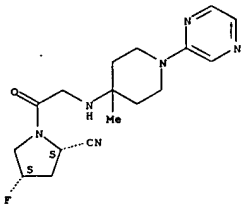
AB 2-Cyanopyrrolidinecarboxamides (shown as I (other Markush formulas shown in claims); X1 and X2 = lower alkylene; X3 = CH2, CHF or CF2; R1 = OR4, NR5R6, :NR7 (variables defined in claims), R2 and R3 = H or lower alkyl; n = 0-4; e.g. (2S)-1-[[(1S,3S,4S,5R)-5-Hydroxy-2-azabicyclo[2.2.2]oct-3-yl]carbonyl]-2-pyrrolidinecarbonitrile hydrochloride (free base shown as II)) or pharmaceutically acceptable salts thereof have activity inhibiting DPP-IV. They are therefore useful in the treatment of conditions mediated by DPP-IV, such as NIDDM. IC50 values for inhibiting DPP-IV are tabulated for 6 claimed compds. (e.g. 8.5 nM for II). A method of preparation is claimed (deprotection of N-protected I) and 46 example prepns. are included. For example, (2S)-1-[[(1S,3S,4S,5S,6R)-5,6-dihydroxy-2-azabicyclo[2.2.2]oct-3-yl]carbonyl]-2-pyrrolidinecarbonitrile hydrochloride was prepared in 5 steps starting from Et (1S,3S,4R)-2-((1R)-1-phenylethyl)-2-azabicyclo[2.2.2]oct-5-ene-3-carboxylate and involving intermediates Et (1S,3S,4S,5S,6R)-5,6-dihydroxy-2-((1R)-1-phenylethyl)-2-azabicyclo[2.2.2]octane-3-carboxylate, Et (1S,3S,4S,5S,6R)-5,6-dihydroxy-2-azabicyclo[2.2.2]octane-3-carboxylate, (1S,3S,4S,5S,6R)-2-(tert-Butoxycarbonyl)-5,6-dihydroxy-2-azabicyclo[2.2.2]octane-3-carboxylic acid and tert-Bu (1S,3S,4S,5S,6R)-3-[[(2S)-2-cyano-1-pyrrolidinyl]carbonyl]-5,6-dihydroxy-2-azabicyclo[2.2.2]octane-2-carboxylate.

IT 851389-46-3P, (2S,4S)-4-Fluoro-1-[[[4-methyl-1-(2-pyrazinyl)-4-piperidinyl]amino]acetyl]-2-pyrrolidinecarbonitrile 851390-47-1P, (2S,4S)-4-Fluoro-1-[[[1-methyl-1,2,3,4-tetrahydro-4-quinolinyl]amino]acetyl]-2-pyrrolidinecarbonitrile 851455-62-4P, (2S,4S)-4-Fluoro-1-[[[(1R,5S)-3-methyl-8-(2-pyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-2-pyrrolidinecarbonitrile
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of azabicycle-containing 2-cyanopyrrolidinecarboxamides as dipeptidyl peptidase-IV inhibitors useful for treating non-insulin-dependent diabetes mellitus)

RN 851389-46-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(4-methyl-1-pyrazinyl-4-piperidinyl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

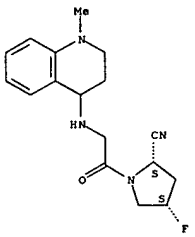
Absolute stereochemistry.

L4 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



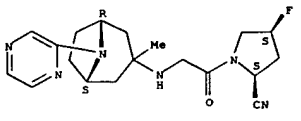
RN 851390-47-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(1,2,3,4-tetrahydro-1-methyl-4-quinolinyl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 851455-62-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(1R,5S)-3-methyl-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

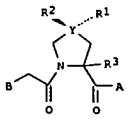
Absolute stereochemistry.



L4 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 29 Apr 2005
ACCESSION NUMBER: 2005:371255 HCAPLUS
DOCUMENT NUMBER: 142:430527
TITLE: Preparation of 2-pyrrolidinecarboxylic acid-based compounds as novel inhibitors of dipeptidyl peptidase-IV (DPP-IV)
INVENTOR(S): Lee, Chang-seok; Koo, Ki Dong; Koh, Jong Sung; Kim, Sungsub; Kim, Dong-myung; Kim, Min-jung; Kim, Bongchan; Yoon, Suk Kyoon; Kim, Sungji; Yim, Hyeon Joo; Hur, Gwong-cheung; Lee, Sun Hwa; Han, Hee Oon; Kim, Kyoung-hee; Kim, Geun Tae; Kwon, Oh Hwan; Kwon, Tae-sik; Lee, Hee Bong; Chung, Hee-kyung; Kim, Misun; Lim, Dongchul; Kim, Yeon Chul; Kim, Sungho
PATENT ASSIGNEE(S): Lg Life Sciences Ltd., S. Korea
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037828	A1	20050428	WO 2004-KR2679	20041020
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2005037973	A	20050425	KR 2004-83793	20041020
PRIORITY APPLN. INFO.:			KR 2003-72962 A	20031020
			KR 2003-72977 A	20031020
			KR 2004-36439 A	20040521

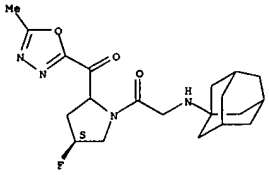
OTHER SOURCE(S): MARPAT 142:430527
GI



I

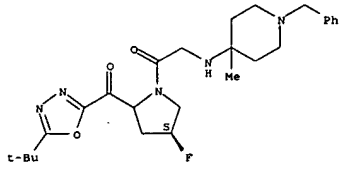
AB The invention relates to pyrrolidine-based compds. I [A is 1,3,4-oxa(or thia)diazol-2-yl or 1,2,4-oxadiazol-3(or 5)-yl which may be substituted; B is R5R6N(CH2)0-2,, where R5, R6 are independently H, (un)saturated alkyl or cycloalkyl, aryl, heteroaryl or heterocyclyl; Y is C and R1, R2 are independently H or halo; or Y is O or S and R1, R2 are null; R3 is H or alkyl] which have good inhibitory activity against DPP-IV and can be used in formulations to treat or prevent DPP-IV related diseases, e.g., diabetes mellitus and obesity. Thus, 2-(2-hydroxy-1,1-dimethylethylamino)-1-[(S,S)-4-fluoro-2-[5-tert-butyl-[1,3,4]oxadiazole-2-carbonyl]pyrrolidin-1-yl]ethanone was prepared by a multistep procedure starting from Boc-protected proline and showed IC50 = 22 nM for inhibition of DPP-IV.
IT 851027-08-2P 851027-48-0P 851027-49-1P
851027-50-4P 851027-51-5P 851028-53-0P
851028-55-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidinecarboxylic acid-based compds. as novel inhibitors of dipeptidyl peptidase-IV (DPP-IV))
RN 851027-08-2 HCAPLUS
CN Pyrrolidine, 4-fluoro-2-[(5-methyl-1,3,4-oxadiazol-2-yl)carbonyl]-1-[(tricyclo[3.3.1.13,7]dec-1-ylamino)acetyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



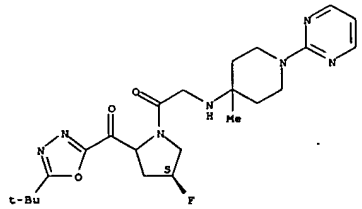
RN 851027-48-0 HCAPLUS
CN Pyrrolidine, 2-[[5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2-yl]carbonyl]-4-fluoro-1-[[[4-methyl-1-(phenylmethyl)-4-piperidinyl]amino]acetyl]-, (4S)- (9CI) (CA INDEX NAME)

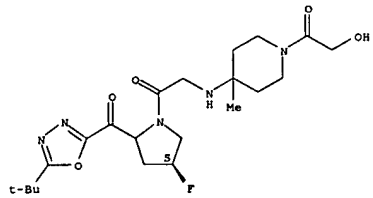
Absolute stereochemistry.



RN 851027-49-1 HCAPLUS
CN Pyrrolidine, 2-[[5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2-yl]carbonyl]-4-fluoro-1-[[[4-methyl-1-(2-pyrimidinyl)-4-piperidinyl]amino]acetyl]-, (4S)- (9CI) (CA INDEX NAME)

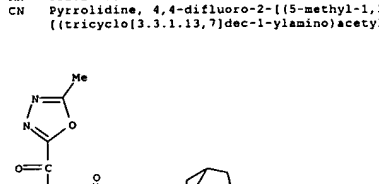
Absolute stereochemistry.



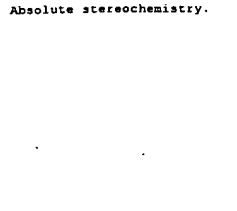


RN 851027-50-4 HCAPLUS
CN Piperidine, 4-[[2-[(4S)-2-[[5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2-yl]carbonyl]-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-1-(hydroxyacetyl)-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



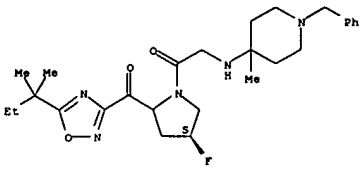
RN 851027-51-5 HCAPLUS
CN Pyrrolidine, 4,4-difluoro-2-[(5-methyl-1,3,4-oxadiazol-2-yl)carbonyl]-1-[(tricyclo[3.3.1.13,7]dec-1-ylamino)acetyl]- (9CI) (CA INDEX NAME)



RN 851028-53-0 HCAPLUS
CN Pyrrolidine, 2-[[5-(1,1-dimethylpropyl)-1,2,4-oxadiazol-3-yl]carbonyl]-4-fluoro-1-[[[4-methyl-1-(phenylmethyl)-4-piperidinyl]amino]acetyl]-, (4S)- (9CI) (CA INDEX NAME)

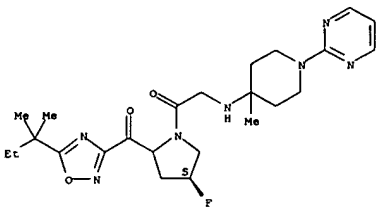
Absolute stereochemistry.

L4 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 851028-55-2 HCAPLUS
CN Pyrrolidine, 2-[[5-(1,1-dimethylpropyl)-1,2,4-oxadiazol-3-yl]carbonyl]-4-fluoro-1-[[[4-methyl-1-(2-pyrimidinyl)-4-piperidinyl]amino]acetyl]-, (4S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 11 Mar 2005
ACCESSION NUMBER: 2005:216813 HCAPLUS
DOCUMENT NUMBER: 142:298122
TITLE: Preparation of pyrrolidinecarbonitrile compounds and analogs for DPP-IV enzyme inhibition
INVENTOR(S): Aranyi, Peter; Bata, Imre; Batori, Sandor; Boronkay, Eva; Bovy, Philippe; Kapui, Zoltan; Susan, Edit; Szabo, Tibor; Urban-szabo, Katalin; Varga, Marton
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.; Sanofi Aventis
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021536	A2	20050310	WO 2004-HU88	20040827
WO 2005021536	A3	20051013		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004268832	A1	20050310	AU 2004-268832	20040827
CA 2537123	A1	20050310	CA 2004-2537123	20040827
EP 1664031	A2	20060607	EP 2004-769087	20040827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1845921	A	20061011	CN 2004-80024974	20040827
BR 2004013973	A	20061031	BR 2004-13973	20040827
US 2006276487	A1	20061207	US 2006-364154	20060228
PRIORITY APPLN. INFO.:			HU 2003-2788 A	20030829
			WO 2004-HU88 W	20040827

OTHER SOURCE(S): MARPAT 142:298122
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

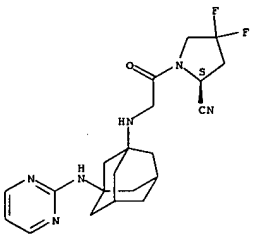
AB A variety of compds. of the general formula R-B-NHCH2CO-Z-CN [R = mono or bicyclic (hetero)aryl, substituted Ph, R1aCH2, R1a = H, C1-C4 alkyl, Ph, PhCH2, pyridyl, quinolinyl, thienyl, C1-C4 alkoxy, cyano, etc.; R = R1aR2CH2, R2 = H, Me; R = R1bCO, R2 = C1-C4 alkyl, Ph, PhCH2, PhCH2CH2, naphthyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinolinyl, pyridyl, quinazolinyl, quinoxalinyl; R = 4-MeC6H4SO2; B = rings Q, Q1, Q2, Q3; Z = ring Q4, X = CF2, CHF, CH2, S, O] were prepd. For example, 1,3-diaminoadamantane reacted with p-anisoyl chloride to give N-(3-amino-1-adamantyl)-4-methoxybenzamide which was condensed with (2S)-1-(chloroacetyl)-4,4-difluoropyrrolidine-2-carbonitrile to give one of the title compds. I. The compds. are intended to be used as DPP-IV enzyme inhibitors and to treat diseases related to DPP-IV enzyme concn.

IT 847795-87-3P 847795-93-1P 847795-95-3P
847796-01-4P 847796-07-0P 847796-08-1P
847796-11-6P 847796-12-7P 847796-14-9P
847796-15-0P 847796-16-1P 847796-17-2P
847796-19-4P 847796-20-7P 847796-22-9P
847796-24-1P 847796-25-2P 847796-26-3P
847796-27-4P 847796-29-6P 847796-30-9P
847796-31-0P 847796-32-1P 847796-33-2P
847796-34-3P 847796-37-6P 847796-38-7P
847796-40-1P 847796-41-2P 847796-42-3P
847796-45-6P 847796-46-7P 847796-47-8P
847796-84-3P 847796-85-4P 847796-86-5P
847796-87-6P 847796-88-7P 847796-91-2P
847796-92-3P 847796-93-4P 847796-94-5P
847796-95-6P 847796-96-7P 847796-97-8P
847796-98-9P 847796-99-0P 847797-00-6P
847797-01-7P 847797-02-8P 847797-03-9P
847797-05-1P 847797-06-2P 847797-07-3P
847797-08-4P 847797-09-5P 847797-10-8P
847797-11-9P 847797-12-0P 847797-13-1P
847797-14-2P 847797-15-3P 847797-16-4P
847797-17-5P 847862-29-7P 847862-30-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidinecarbonitriles and related compds. for DPP-IV enzyme inhibition)

RN 847795-87-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-(2-pyrimidinylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

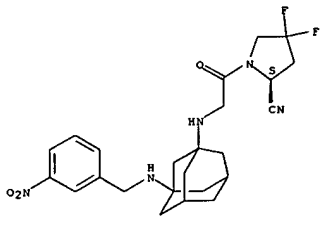
L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 847795-93-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[[(3-nitrophenyl)methyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, trihydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

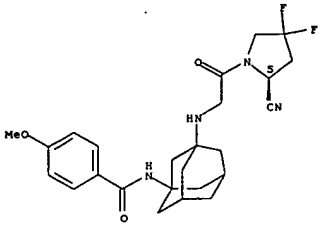


●3 HCl

RN 847795-95-3 HCAPLUS
CN Benzamide, N-[3-[[2-[(2S)-2-cyano-4,4-difluoro-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]-4-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

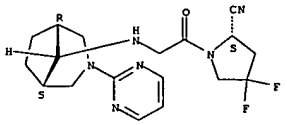
L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 847796-01-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(8-syn)-3-(2-pyrimidinyl)-3-azabicyclo[3.2.1]oct-8-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

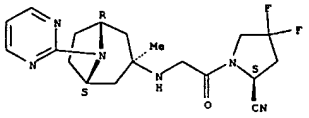
Absolute stereochemistry.



RN 847796-07-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-3-methyl-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

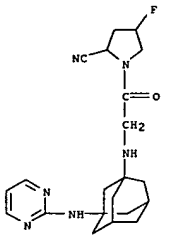
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



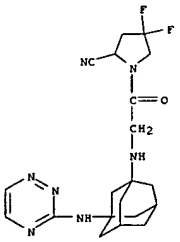
●2 HCl

RN 847796-08-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[3-(2-pyrimidinylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]- (9CI) (CA INDEX NAME)



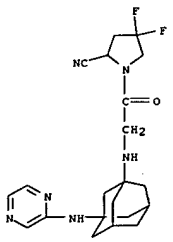
RN 847796-11-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-(1,2,4-triazin-3-ylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●3 HCl

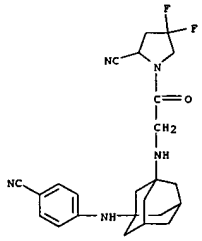
RN 847796-12-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-(pyrazinylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

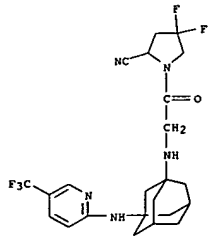
RN 847796-14-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-[(4-cyanophenyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-4,4-difluoro-, trihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●3 HCl

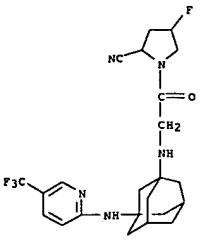
RN 847796-15-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[[5-(trifluoromethyl)-2-pyridinyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

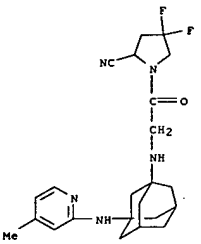
RN 847796-16-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[3-[[5-(trifluoromethyl)-2-pyridinyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●3 HCl

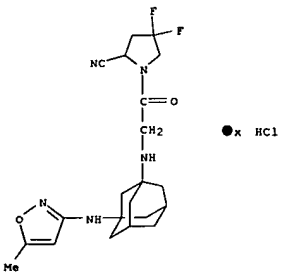
RN 847796-17-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[(4-methyl-2-pyridinyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

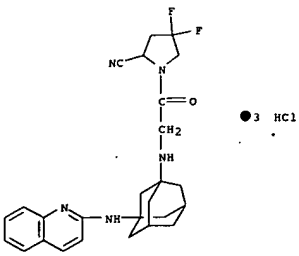
RN 847796-19-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-(2-thiazolylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-,

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
hydrochloride (9CI) (CA INDEX NAME)



●x HCl

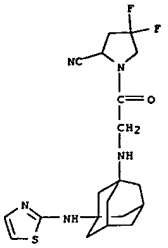
RN 847796-24-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-(2-quinolinylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

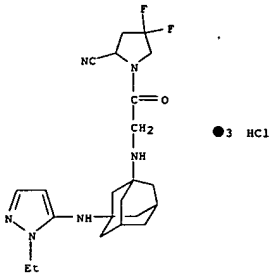
RN 847796-25-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[3-(2-quinolinylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

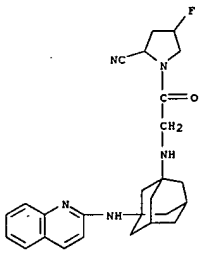
RN 847796-20-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-[(1-ethyl-1H-pyrazol-5-yl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-4,4-difluoro-, trihydrochloride (9CI) (CA INDEX NAME)



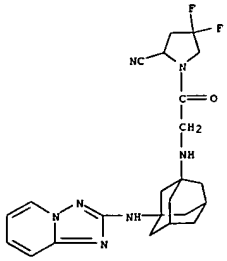
●3 HCl

RN 847796-22-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[(5-methyl-3-isoxazolyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-,

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



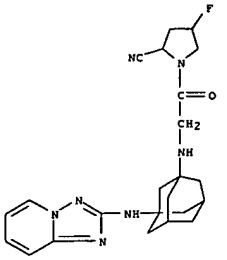
RN 847796-26-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)



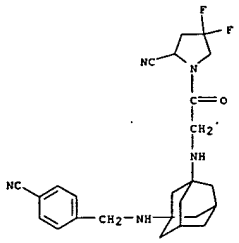
●3 HCl

RN 847796-27-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[3-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



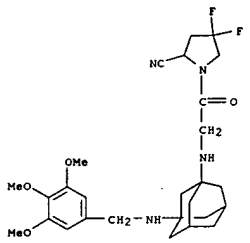
RN 847796-29-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-[[[4-cyanophenyl)methyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-4,4-difluoro-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

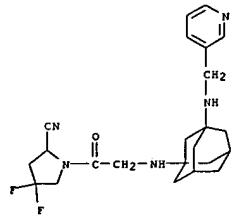
RN 847796-30-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[[[4-(trifluoromethyl)phenyl]methyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

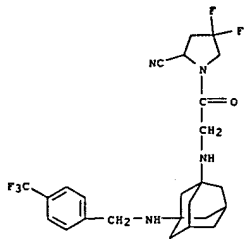
RN 847796-33-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[(3-pyridinylmethyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

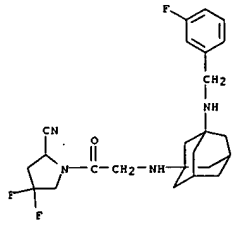
RN 847796-34-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[(3-pyridazinylmethyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, pentahydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●3 HCl

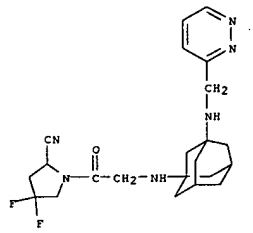
RN 847796-31-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[[(3-fluorophenyl)methyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

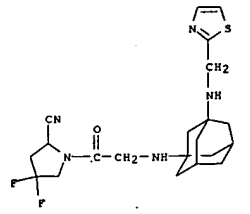
RN 847796-32-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[[(3,4,5-trimethoxyphenyl)methyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-,

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●5 HCl

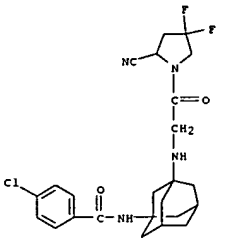
RN 847796-37-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[(2-thiazolylmethyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

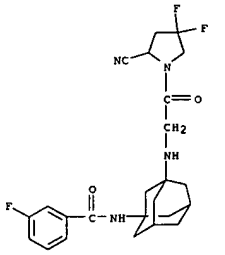
RN 847796-38-7 HCAPLUS
CN Benzamide, 4-chloro-N-[3-[[2-(2-cyano-4,4-difluoro-1-pyrrolidinyl)-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● HCl

RN 847796-40-1 HCAPLUS
CN Benzamide, N-[3-[[2-(2-cyano-4,4-difluoro-1-pyrrolidinyl)-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]-3-fluoro-, monohydrochloride (9CI) (CA INDEX NAME)



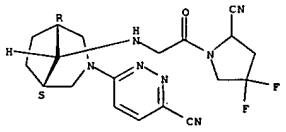
● HCl

RN 847796-41-2 HCAPLUS
CN 2-Propenamide, N-[3-[[2-(2-cyano-4,4-difluoro-1-pyrrolidinyl)-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]-3-phenyl-, dihydrochloride, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

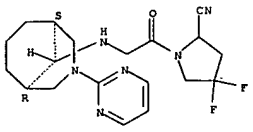
Relative stereochemistry.



● HCl

RN 847796-46-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(9-syn)-3-(2-pyrimidinyl)-3-azabicyclo[3.3.1]non-9-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

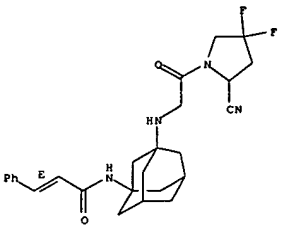


●2 HCl

RN 847796-47-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(9-syn)-3-(6-cyano-3-pyridazinyl)-3-azabicyclo[3.3.1]non-9-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

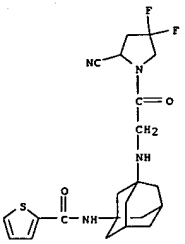
Relative stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

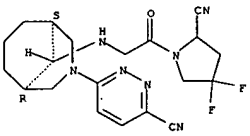
RN 847796-42-3 HCAPLUS
CN 2-Thiophenecarboxamide, N-[3-[[2-(2-cyano-4,4-difluoro-1-pyrrolidinyl)-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 847796-45-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(8-syn)-3-(6-cyano-3-pyridazinyl)-3-azabicyclo[3.2.1]oct-8-yl]amino]acetyl]-4,4-difluoro-, monohydrochloride (9CI) (CA INDEX NAME)

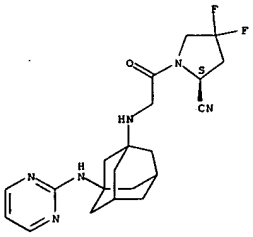
L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 847796-84-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-(2-pyrimidinylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

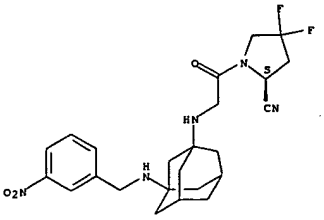
Absolute stereochemistry.



RN 847796-85-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[[(3-nitrophenyl]methyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

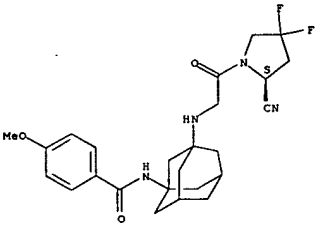
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847796-86-5 HCAPLUS
CN Benzamide, N-[3-[[2-[(2S)-2-cyano-4,4-difluoro-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]-4-methoxy- (9CI) (CA INDEX NAME)

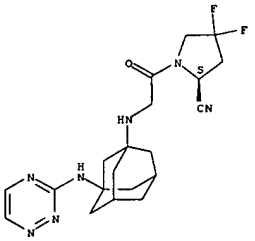
Absolute stereochemistry.



RN 847796-87-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-3-methyl-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

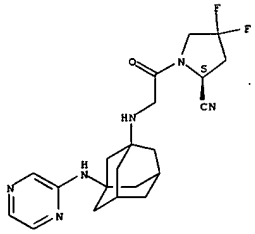
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847796-92-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-(pyrazinylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

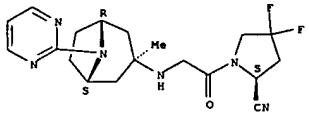
Absolute stereochemistry.



RN 847796-93-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-[(4-cyanophenyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-4,4-difluoro-, (2S)- (9CI) (CA INDEX NAME)

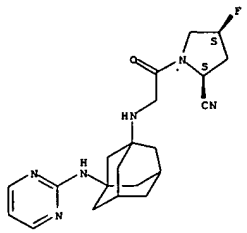
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847796-88-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[3-(2-pyrimidinylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

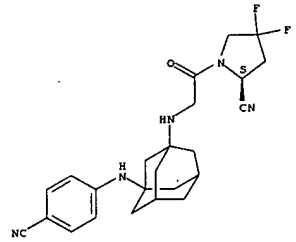
Absolute stereochemistry.



RN 847796-91-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-(1,2,4-triazin-3-ylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

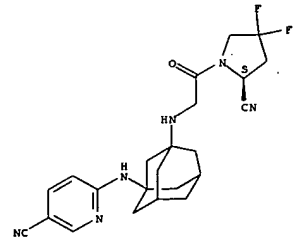
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847796-94-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-[(5-cyano-2-pyridinyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-4,4-difluoro-, (2S)- (9CI) (CA INDEX NAME)

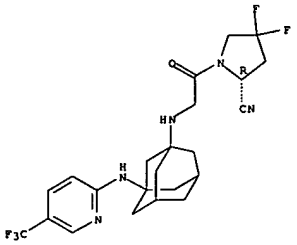
Absolute stereochemistry.



RN 847796-95-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[(5-(trifluoromethyl)-2-pyridinyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2R)- (9CI) (CA INDEX NAME)

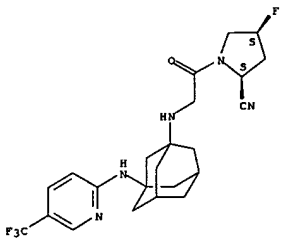
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847796-96-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-{[[3-[[5-(trifluoromethyl)-2-pyridinyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S,4S)-(9CI) (CA INDEX NAME)

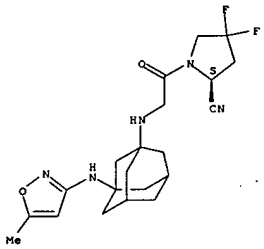
Absolute stereochemistry.



RN 847796-97-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-(2-thiazolylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

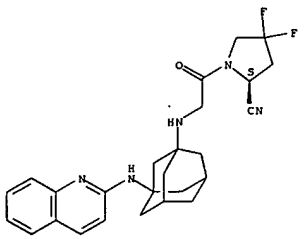
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847797-00-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-(2-quinolinylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

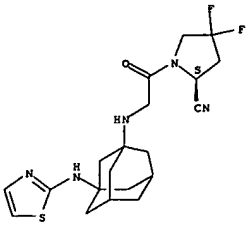
Absolute stereochemistry.



RN 847797-01-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[3-(2-quinolinylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S,4S)-(9CI) (CA INDEX NAME)

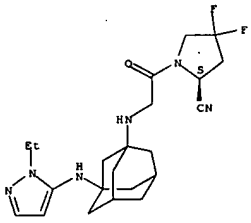
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847796-98-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-{[[3-[(1-ethyl-1H-pyrazol-5-yl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-4,4-difluoro-, (2S)-(9CI) (CA INDEX NAME)

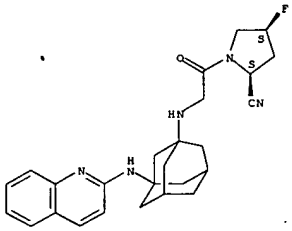
Absolute stereochemistry.



RN 847796-99-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[(5-methyl-3-isoxazolyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

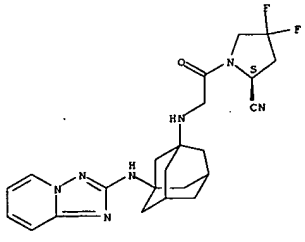
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847797-02-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)-(9CI) (CA INDEX NAME)

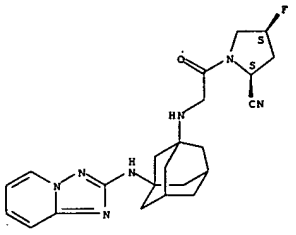
Absolute stereochemistry.



RN 847797-03-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-{[[3-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

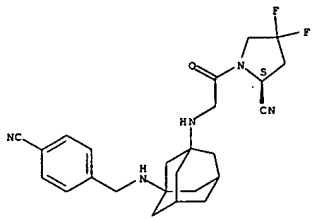
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847797-05-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-[[[4-cyanophenyl)methyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-4,4-difluoro-, (2S)- (9CI) (CA INDEX NAME)

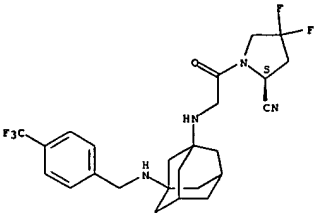
Absolute stereochemistry.



RN 847797-06-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[[[4-(trifluoromethyl)phenyl]methyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

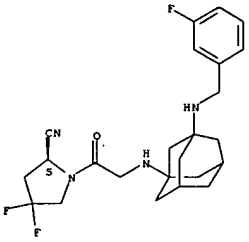
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847797-07-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[[(3-fluorophenyl)methyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

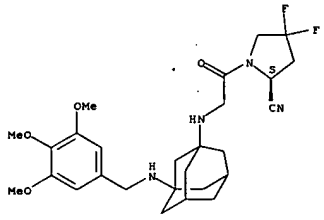
Absolute stereochemistry.



RN 847797-08-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[[(3,4,5-trimethoxyphenyl)methyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

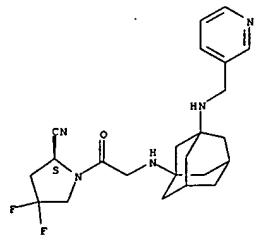
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 847797-09-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[(3-pyridinylmethyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

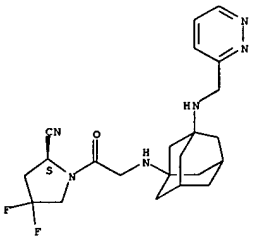
Absolute stereochemistry.



RN 847797-10-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[(3-pyridazinylmethyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)-
(9CI) (CA INDEX NAME)

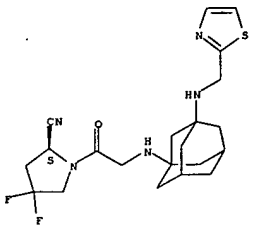
Absolute stereochemistry.

L4 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



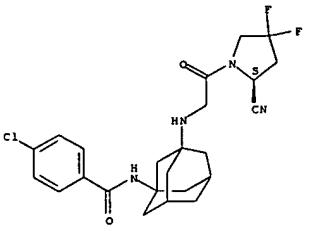
RN 847797-11-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[3-[(2-thiazolylmethyl)amino]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



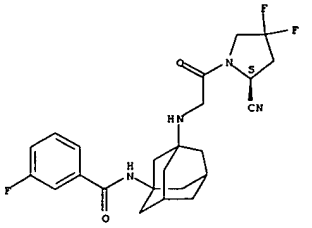
RN 847797-12-0 HCAPLUS
CN Benzamide, 4-chloro-N-[3-[[2-[(2S)-2-cyano-4,4-difluoro-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



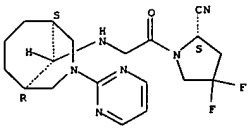
RN 847797-13-1 HCAPLUS
CN Benzamide, N-[3-[[2-[(2S)-2-cyano-4,4-difluoro-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]-3-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



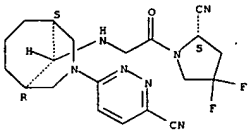
RN 847797-14-2 HCAPLUS
CN 2-Propenamide, N-[3-[[2-[(2S)-2-cyano-4,4-difluoro-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]-3-phenyl-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



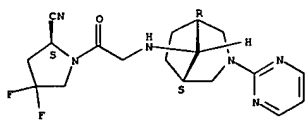
RN 847797-17-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(9-syn)-3-(6-cyano-3-pyridazinyl)-3-azabicyclo[3.3.1]non-9-yl]amino]acetyl]-4,4-difluoro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 847862-29-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(8-anti)-3-(2-pyrimidinyl)-3-azabicyclo[3.2.1]oct-8-yl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

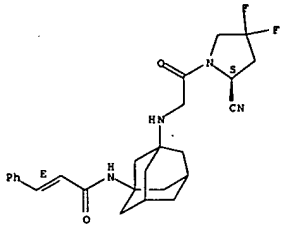
Absolute stereochemistry.



●2 HCl

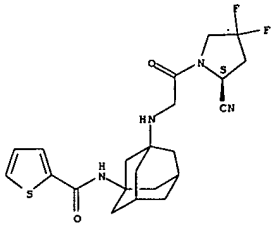
RN 847862-30-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(8-anti)-3-(2-pyrimidinyl)-3-azabicyclo[3.2.1]oct-8-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



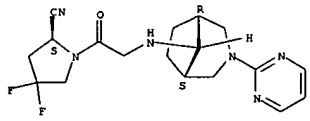
RN 847797-15-3 HCAPLUS
CN 2-Thiophenecarboxamide, N-[3-[[2-[(2S)-2-cyano-4,4-difluoro-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 847797-16-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(9-syn)-3-(2-pyrimidinyl)-3-azabicyclo[3.3.1]non-9-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 19 Nov 2004
ACCESSION NUMBER: 2004:996160 HCAPLUS
DOCUMENT NUMBER: 141:410811
TITLE: Preparation of 1-(2-aminoacetyl)-2-cyanopyrrolidines as dipeptidyl peptidase-IV inhibitors for treatment of NIDDM
INVENTOR(S): Shima, Ichiro; Kurosaki, Toshio; Wada, Aiko
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co. Ltd., Japan
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

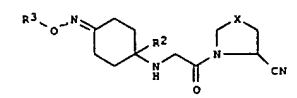
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099185	A1	20041118	WO 2004-JP6568	20040510

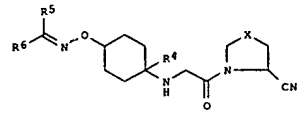
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

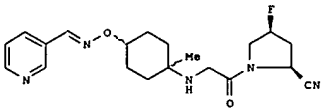
PRIORITY APPLN. INFO.: AU 2003-902260 A 20030509

OTHER SOURCE(S): MARPAT 141:410811
GI

L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)







AB Title compds. I and II [wherein X = CHF, CF2; R2 = alkyl; R3 = (un)substituted cycloalkyl, (hetero)arylalkyl; R4 = alkyl; R5 = H, alkyl; R6 = (un)substituted (cyclo)alkyl, (hetero)aryl; or CR5R6 = cycloalkyl; and pharmaceutically acceptable salts thereof] were prepared as dipeptidyl peptidase-IV (DPP-IV) inhibitors. For example, coupling of tert-Bu 4-(aminooxy)-1-methylcyclohexylcarbamate with nicotinaldehyde, deprotection of the amine, and alkylation with (2S,4S)-1-chloroacetyl-4-fluoro-2-pyrrolidinecarbonitrile, afforded III. The latter inhibited human plasma DPP-IV with an IC50 value of 14 nM. Thus, I, II, and their pharmaceutical compns. are useful in the treatment of conditions mediated by DPP-IV, such as non-insulin dependent diabetes mellitus (NIDDM).

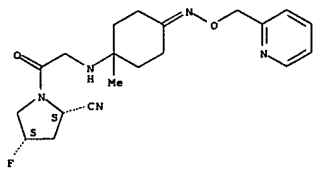
IT 792913-88-3P, (2S,4S)-4-Fluoro-1-[[[1-methyl-4-[(2-pyridinylmethoxy)imino]cyclohexyl]amino]acetyl]-2-pyrrolidinecarbonitrile dihydrochloride 792913-91-8P, (2S,4S)-4-Fluoro-1-[[[1-methyl-4-[(3-pyridinylmethoxy)imino]cyclohexyl]amino]acetyl]-2-pyrrolidinecarbonitrile dihydrochloride 792913-95-2P, (2S,4S)-4-Fluoro-1-[[[1-methyl-4-[[(6-methyl-2-pyridinyl)methoxy]imino]cyclohexyl}amino]acetyl]-2-pyrrolidinecarbonitrile dihydrochloride 792913-99-6P, (2S,4S)-4-Fluoro-1-[[[1-methyl-4-[[(2-methyl-3-pyridinyl)methoxy]imino]cyclohexyl]amino]acetyl]-2-pyrrolidinecarbonitrile dihydrochloride 792914-02-4P, (2S,4S)-1-[[[4-[[(6-Chloro-3-pyridinyl)methoxy]imino]-1-methylcyclohexyl]amino]acetyl]-4-fluoro-2-pyrrolidinecarbonitrile 792914-07-9P 792914-08-0P, (2S)-4,4-Difluoro-1-[[[1-methyl-4-[(2-pyridinylmethoxy)imino]cyclohexyl]amino]acetyl]-2-

L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

pyrrolidinecarbonitrile dihydrochloride 792914-11-5P 792914-13-7P 792914-15-9P 792914-17-1P 792914-19-3P 792914-22-8P 792914-24-0P 792914-26-2P 792914-28-4P 792914-31-9P 792914-34-2P 792914-36-4P 792914-39-7P 792914-42-2P 792914-44-4P 792914-47-7P 792914-50-2P 793672-40-9P 793672-41-0P 793672-43-2P 793672-44-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DPP-IV inhibitor; prepn. of pyrrolidinecarbonitriles as DPP-IV inhibitors for treatment of NIDDM)

RN 792913-88-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-methyl-4-[(2-pyridinylmethoxy)imino]cyclohexyl]amino]acetyl]-, dihydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

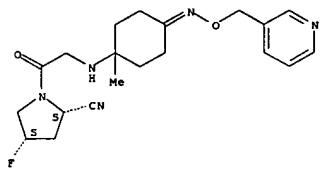


●2 HCl

RN 792913-91-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-methyl-4-[(3-pyridinylmethoxy)imino]cyclohexyl]amino]acetyl]-, dihydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

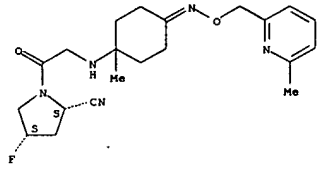
L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 792913-95-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-methyl-4-[[(6-methyl-2-pyridinyl)methoxy]imino]cyclohexyl]amino]acetyl]-, dihydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

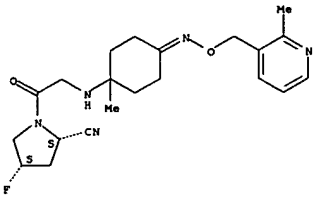


●2 HCl

RN 792913-99-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-methyl-4-[[(2-methyl-3-pyridinyl]methoxy]imino]cyclohexyl]amino]acetyl]-, dihydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

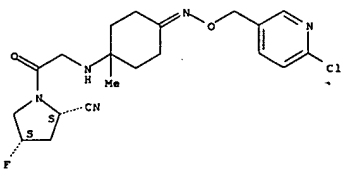
L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 792914-02-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[(4-[[(6-chloro-3-pyridinyl)methoxy]imino]-1-methylcyclohexyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

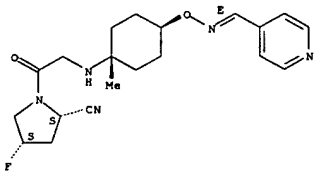
Absolute stereochemistry.



RN 792914-07-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-(2-pyridinylmethylene)amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

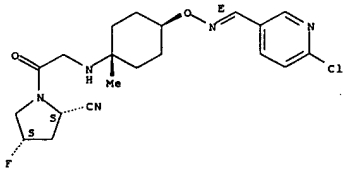
Absolute stereochemistry.
Double bond geometry as shown.

L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



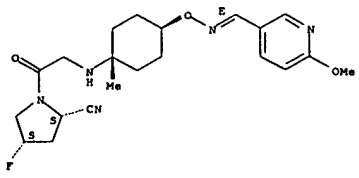
RN 792914-13-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[[(E)-[(6-chloro-3-pyridinyl)methylene]amino]oxy]-1-methylcyclohexyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

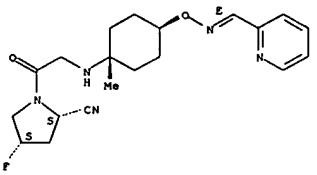


RN 792914-15-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-4-[[(E)-[(6-methoxy-3-pyridinyl)methylene]amino]oxy]-1-methylcyclohexyl]amino]acetyl]-, (2S,4S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

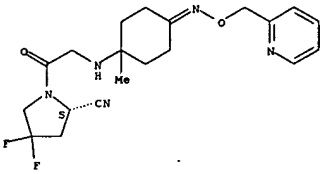


L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 792914-08-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-methyl-4-[(2-pyridinylmethoxy)imino]cyclohexyl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

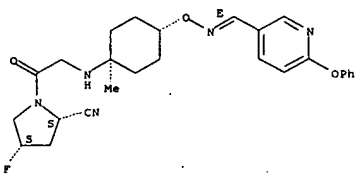
RN 792914-11-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-(4-pyridinylmethylene)amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

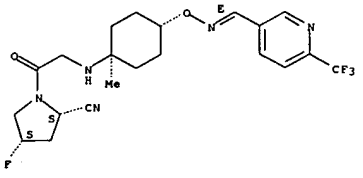
RN 792914-17-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-[(6-phenoxy-3-pyridinyl)methylene]amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 792914-19-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-[(6-(trifluoromethyl)-3-pyridinyl]methylene]amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

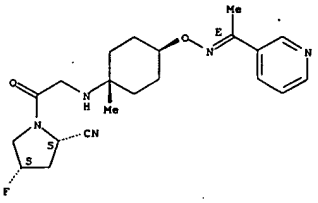
Absolute stereochemistry.
Double bond geometry as shown.



RN 792914-22-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-[1-(3-pyridinyl)ethylidene]amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

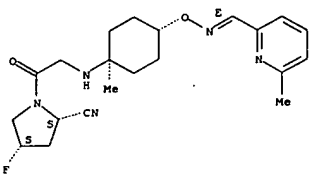
Absolute stereochemistry.
Double bond geometry as shown.

L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 792914-24-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-[(6-methyl-2-pyridinyl)methylene]amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

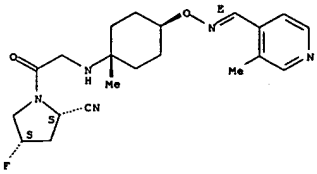
Absolute stereochemistry.
Double bond geometry as shown.



RN 792914-26-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-[(3-methyl-4-pyridinyl)methylene]amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

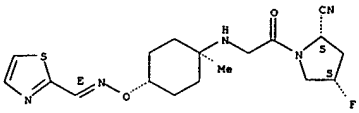
Absolute stereochemistry.
Double bond geometry as shown.

L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



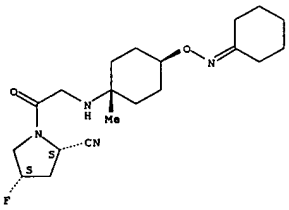
RN 792914-28-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-(2-thiazolylmethylene)amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



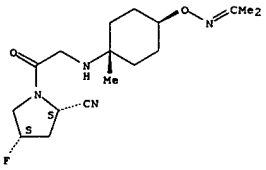
RN 792914-31-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(cyclohexylideneamino)oxy]-1-methylcyclohexyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



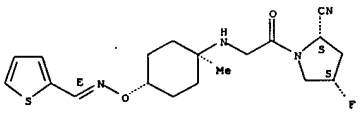
L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 792914-34-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(1-methylethylidene)amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 792914-36-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-(2-thienylmethylene)amino]oxy]cyclohexyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

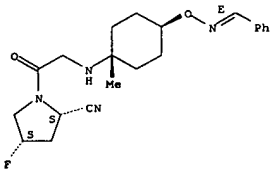


● HCl

RN 792914-39-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-(phenylmethylene)amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

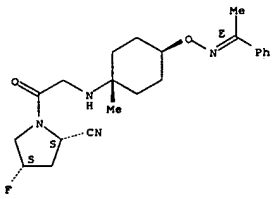
Absolute stereochemistry.
Double bond geometry as shown.

L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



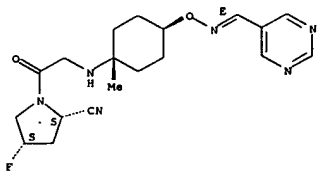
RN 792914-42-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-(1-phenylethylidene)amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 792914-44-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-1-methyl-4-[[(E)-(5-pyrimidinylmethylene)amino]oxy]cyclohexyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

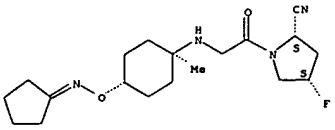
Absolute stereochemistry.
Double bond geometry as shown.



L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

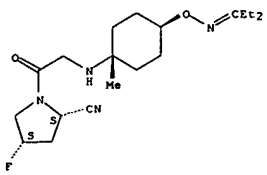
RN 792914-47-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(cyclopentylideneamino)oxy]-1-methylcyclohexyl]amino]acetyl]-4-fluoro-, (2S,4S)-. (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 792914-50-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[[(1-ethylpropylidene)amino]oxy]-1-methylcyclohexyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

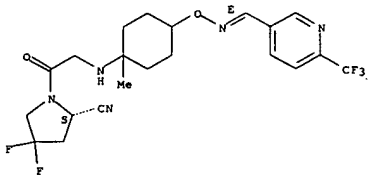
Absolute stereochemistry.



RN 793672-40-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-methyl-4-[[(E)-(3-pyridinylmethylene)amino]oxy]cyclohexyl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

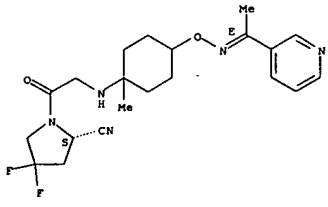
L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 793672-44-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-methyl-4-[[(E)-[1-(3-pyridinyl)ethylidene]amino]oxy]cyclohexyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

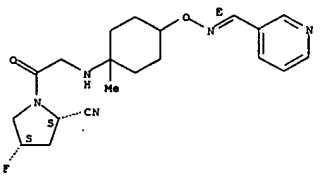


●2 HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

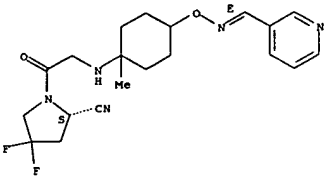
FORMAT

L4 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 793672-41-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-methyl-4-[[(E)-(3-pyridinylmethylene)amino]oxy]cyclohexyl]amino]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 793672-43-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-methyl-4-[[(E)-[[6-(trifluoromethyl)-3-pyridinyl]methylene]amino]oxy]cyclohexyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L4 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 02 Sep 2004
ACCESSION NUMBER: 2004:717809 HCAPLUS
DOCUMENT NUMBER: 141:225305
TITLE: Preparation of 4-substituted-2-cyanopyrrolidine derivatives, pharmaceutical compositions and dipeptidyl peptidase IV inhibitors containing them, and their uses
INVENTOR(S): Toyama, Yasushi; Yokota, Masayuki; Yamamoto, Fuyuka; Kosakai, Kazuhiro
PATENT ASSIGNEE(S): Kotobuki Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004244412	A	20040902	JP 2003-310185	20030902
PRIORITY APPLN. INFO.:			JP 2003-11181	A 20030120

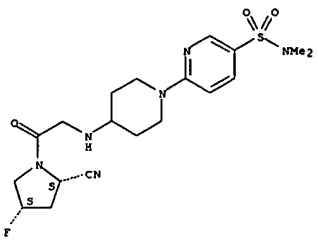
OTHER SOURCE(S): MARPAT 141:225305
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The derivs. I [A = F, CH2F, CHF2, CF3; B = CMeCH2NHD, Q; dotted line represents an optional double bond; D = (un)substituted heterocyclyl; C = H, C1-8 alkyl] or their pharmaceutically acceptable salts, are prepared by reacting II (A = same as above; X = halo, SO2Me, SO2C6H4Me, SO2CF3) with BNH2 (B = same as above). I are useful for treatment of diseases involving dipeptidyl peptidase IV (III), e.g. diabetes, obesity, HIV infection, metastasis, skin diseases, prostatic hypertrophy, pericementitis, autoimmune diseases, etc. III inhibitors are especially useful for treatment of type 2 diabetes, because III inactivates an insulin secretagogue GLP-1. Thus, (2S,4S)-1-{3-[{5-dimethylaminosulfonylpyridin-2-yl}amino]-2-methylpropylamino}acetyl-4-fluoro-2-cyanopyrrolidine (IV), prepared from (2S,4S)-4-fluoropyrrolidine-2-carboxamide trifluoroacetate with 2 steps, inhibited III Caco-2 cells, at IC50 5.7 nM. IV dissolved in a phosphate buffer at 1 + 10-5M and the solution was stored at 25° for 48 h to show 94.4% stability.
IT 748165-39-1P 748165-43-7P 748165-45-9P
748165-47-1P 748165-49-3P 748165-51-7P
748165-73-3P 748165-76-6P 748165-78-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-substituted-2-cyanopyrrolidine derivs. as dipeptidyl peptidase IV inhibitors for treatment of diabetes)
RN 748165-39-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-[5-[(dimethylamino)sulfonyl]-2-pyridinyl]-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA

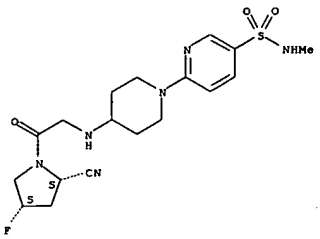
L4 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.



RN 748165-43-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[5-[(methylamino)sulfonyl]-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

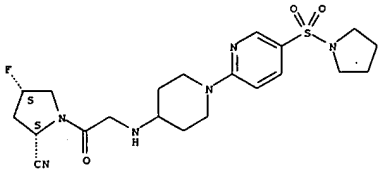
Absolute stereochemistry.



RN 748165-45-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-[5-[(diethylamino)sulfonyl]-2-pyridinyl]-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

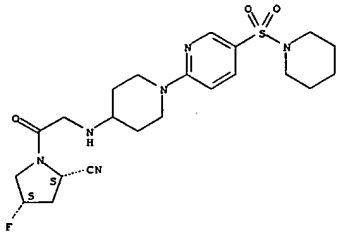
Absolute stereochemistry.

L4 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 748165-51-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[5-(1-piperidinylsulfonyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

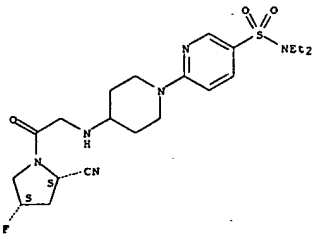
Absolute stereochemistry.



RN 748165-73-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[5-[(methylsulfonyl)amino]-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

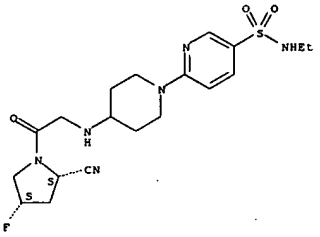
Absolute stereochemistry.

L4 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 748165-47-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-[5-[(ethylamino)sulfonyl]-2-pyridinyl]-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

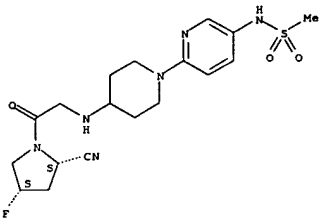
Absolute stereochemistry.



RN 748165-49-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[5-(1-pyrrolidinylsulfonyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

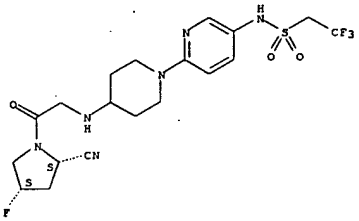
Absolute stereochemistry.

L4 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 748165-76-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[5-[[(2,2,2-trifluoroethyl)sulfonyl]amino]-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

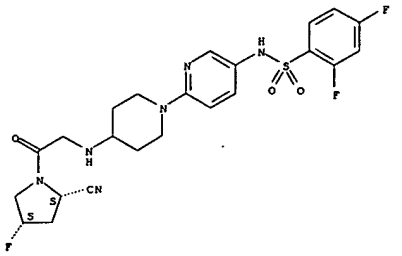
Absolute stereochemistry.



RN 748165-78-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-[5-[[(2,4-difluorophenyl)sulfonyl]amino]-2-pyridinyl]-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



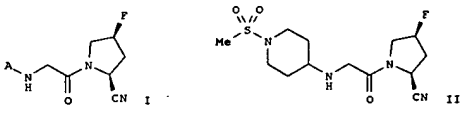
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 01 Feb 2004
ACCESSION NUMBER: 2004:80646 HCAPLUS
DOCUMENT NUMBER: 140:145996
TITLE: Preparation of 2-cyano-4-fluoropyrrolidine derivatives as dipeptidylpeptidase (DPP) IV inhibitors
INVENTOR(S): Hayakawa, Masahiko; Negoro, Kenji; Miyamoto, Satoshi; Suzuki, Takayuki; Maruyama, Tatsuya; Nakano, Ryosuke
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009544	A1	20040129	WO 2003-JP9179	20030718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003281625	A1	20040209	AU 2003-281625	20030718
BR 2003012844	A	20050426	BR 2003-12844	20030718
EP 1541551	A1	20050615	EP 2003-741499	20030718
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CN 1665785	A	20050907	CN 2003-815854	20030718
JP 3778207	B2	20060524	JP 2004-522764	20030718
NZ 537658	A	20060831	NZ 2003-537658	20030718
RU 2288222	C2	20061127	RU 2005-101426	20030718
NO 2005000945	A	20050422	NO 2005-945	20050222

PRIORITY APPLN. INFO.: JP 2002-213654 A 20020723
JP 2002-264450 A 20020910
WO 2003-JP9179 W 20030718

OTHER SOURCE(S): MARPAT 140:145996
GI

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



AB The title 2-cyano-4-fluoropyrrolidine derivs. with general formula of I [where A = (un)substituted heterocyclyl with exclusions] or pharmaceutically acceptable salts thereof are prepared as dipeptidylpeptidase (DPP) IV inhibitors, and are useful for the treatment of insulin-dependent diabetes (type 1 diabetes), in particular, insulin-independent diabetes (type 2 diabetes), insulin resistance disease, and obesity based on the above effect (no data). For example, the compound II•(CHCO2H)2 was prepared in a multi-step synthesis. II showed inhibitory activity with IC50 of 4.2 nM against human DPP IV.

IT 651054-98-7P 651055-01-5P 651055-14-0P
651055-17-3P 651055-20-8P 651055-23-1P
651055-26-4P 651055-29-7P 651055-32-2P
651055-37-7P 651055-41-3P 651055-46-8P
651055-51-5P 651055-56-0P 651055-60-6P
651055-63-9P 651055-77-5P 651055-81-1P
651055-85-5P 651055-88-8P 651055-91-3P
651055-94-6P 651055-97-9P 651056-01-8P
651056-04-1P 651056-07-4P 651056-10-9P
651056-12-1P 651056-15-4P 651056-17-6P
651056-19-8P 651056-21-2P 651056-24-5P
651056-27-8P 651056-30-3P 651056-33-6P
651056-36-9P 651057-02-2P 651057-03-3P
651057-04-4P 651057-05-5P 651057-06-6P
651057-07-7P 651057-08-8P 651057-09-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of (cyano)(fluoro)pyrrolidine derivs. as dipeptidylpeptidase (DPP) IV inhibitors)

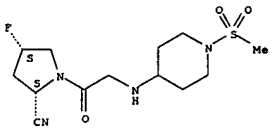
RN 651054-98-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651054-97-6
CMF C13 H21 F N4 O3 S

Absolute stereochemistry.

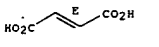
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

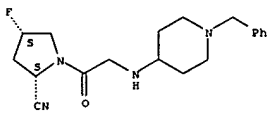


RN 651055-01-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-(phenylmethyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 483365-98-6
CMF C19 H25 F N4 O

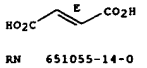
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



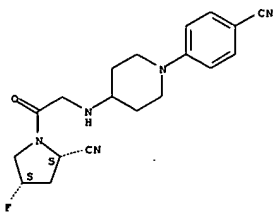
RN 651055-14-0 HCAPLUS

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(4-cyanophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 483366-00-3
CMF C19 H22 F N5 O

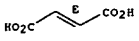
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



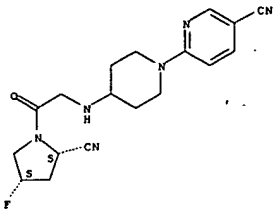
RN 651055-17-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-2-pyridinyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-16-2
CMF C18 H21 F N6 O

Absolute stereochemistry.

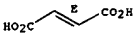
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

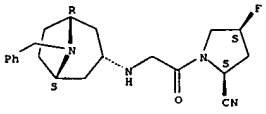


RN 651055-20-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(3-endo)-8-(phenylmethyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-19-5
CMF C21 H27 F N4 O

Absolute stereochemistry.

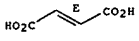


CM 2

CRN 110-17-8

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CMF C4 H4 O4

Double bond geometry as shown.

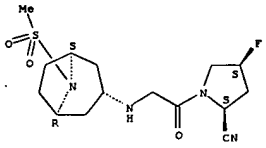


RN 651055-23-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(3-exo)-8-(methylsulfonyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-22-0
CMF C15 H23 F N4 O3 S

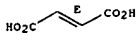
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



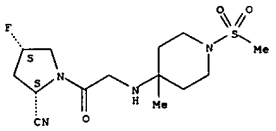
RN 651055-26-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-methyl-1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-25-3
CMF C14 H23 F N4 O3 S

Absolute stereochemistry.

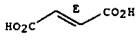
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

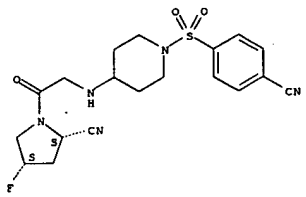


RN 651055-29-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-[(4-cyanophenyl)sulfonyl]-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-28-6
CMF C19 H22 F N5 O3 S

Absolute stereochemistry.

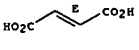


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

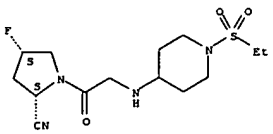


RN 651055-32-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(ethylsulfonyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-31-1
CMF C14 H23 F N4 O3 S

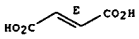
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



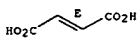
RN 651055-37-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-(propylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-36-6
CMF C15 H25 F N4 O3 S

Absolute stereochemistry.

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

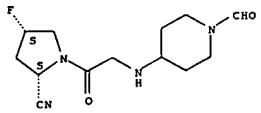


RN 651055-46-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(1-formyl-4-piperidinyl)amino]acetyl]-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-45-7
CMF C13 H19 F N4 O2

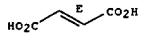
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

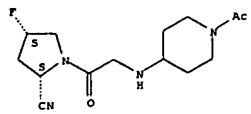


RN 651055-51-5 HCAPLUS
CN 4-Piperidinamine, 1-acetyl-N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

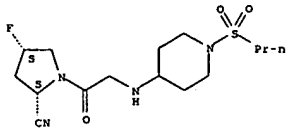
CM 1

CRN 651055-50-4
CMF C14 H21 F N4 O2

Absolute stereochemistry.



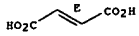
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

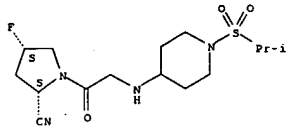


RN 651055-41-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[(1-methylethyl)sulfonyl]-4-piperidinyl]amino]acetyl]-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 483365-94-2
CMF C15 H25 F N4 O3 S

Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

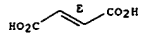
Double bond geometry as shown.

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

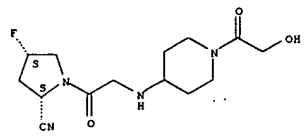


RN 651055-56-0 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(hydroxyacetyl)-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-55-9
CMF C14 H21 F N4 O3

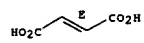
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



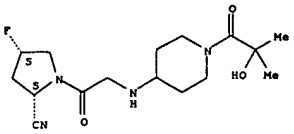
RN 651055-60-6 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(2-hydroxy-2-methyl-1-oxopropyl)-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-59-3
CMF C16 H25 F N4 O3

Absolute stereochemistry.

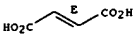
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

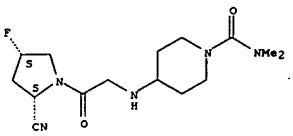


RN 651055-63-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-N,N-dimethyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-62-8
CMF C15 H24 F N5 O2

Absolute stereochemistry.

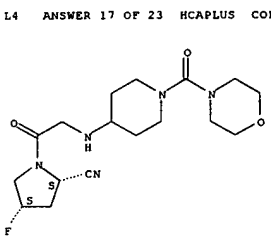


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

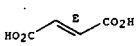
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

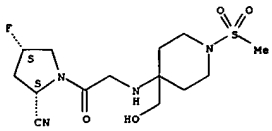


RN 651055-85-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-(hydroxymethyl)-1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-84-4
CMF C14 H23 F N4 O4 S

Absolute stereochemistry.

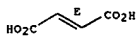


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

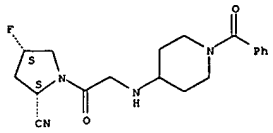


RN 651055-77-5 HCAPLUS
CN 4-Piperidinamine, 1-benzoyl-N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-76-4
CMF C19 H23 F N4 O2

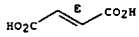
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



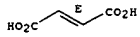
RN 651055-81-1 HCAPLUS
CN Morpholine, 4-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-1-piperidinyl]carbonyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-80-0
CMF C17 H26 F N5 O3

Absolute stereochemistry.

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

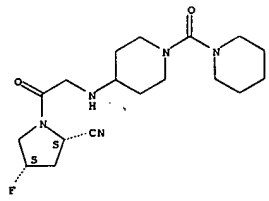


RN 651055-88-8 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(1-piperidinylcarbonyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-87-7
CMF C18 H28 F N5 O2

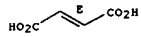
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



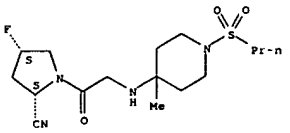
RN 651055-91-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-methyl-1-(propylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-90-2
CMF C16 H27 F N4 O3 S

Absolute stereochemistry.

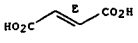
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

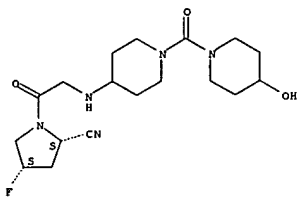


RN 651055-94-6 HCAPLUS
CN 4-Piperidinol, 1-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-1-piperidinyl]carbonyl]-, (2E)-2-butenedioate (1:1) (salt)
(9CI) (CA INDEX NAME)

CM 1

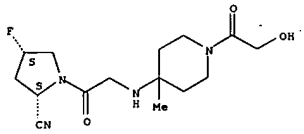
CRN 651055-93-5
CMF C18 H28 F N5 O3

Absolute stereochemistry.



CM 2

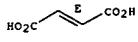
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

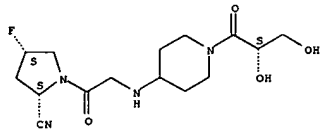


RN 651056-04-1 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-[(2S)-2,3-dihydroxy-1-oxopropyl]-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-03-0
CMF C15 H23 F N4 O4

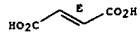
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

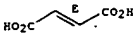
Double bond geometry as shown.



RN 651056-07-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(1-formyl-4-methyl-4-

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

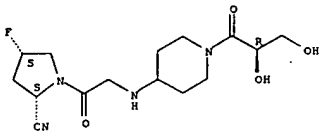


RN 651055-97-9 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-[(2R)-2,3-dihydroxy-1-oxopropyl]-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 651055-96-8
CMF C15 H23 F N4 O4

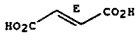
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 651056-01-8 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(hydroxyacetyl)-4-methyl-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-00-7
CMF C15 H23 F N4 O3

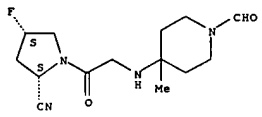
Absolute stereochemistry.

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
piperidinyl]amino]acetyl)-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA
INDEX NAME)

CM 1

CRN 651056-06-3
CMF C14 H21 F N4 O2

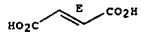
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

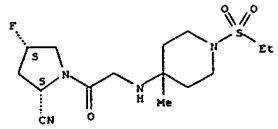


RN 651056-10-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(ethylsulfonyl)-4-methyl-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-09-6
CMF C15 H25 F N4 O3 S

Absolute stereochemistry.

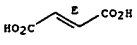


CM 2

CRN 110-17-8

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CMF C4 H4 O4

Double bond geometry as shown.

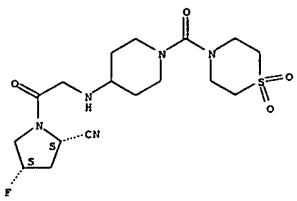


RN 651056-12-1 HCAPLUS
CN Thiomorpholine, 4-[[4-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-1-piperidinyl]carbonyl]-, 1,1-dioxide, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-11-0
CMF C17 H26 F N5 O4 S

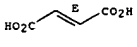
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

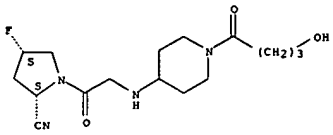


RN 651056-15-4 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(4-hydroxy-1-oxobutyl)-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CRN 651056-14-3
CMF C16 H25 F N4 O3

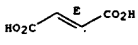
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

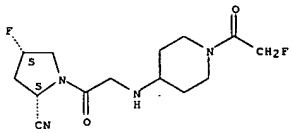


RN 651056-17-6 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(fluoroacetyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-16-5
CMF C14 H20 F2 N4 O2

Absolute stereochemistry.

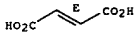


CM 2

CRN 110-17-8
CMF C4 H4 O4

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Double bond geometry as shown.

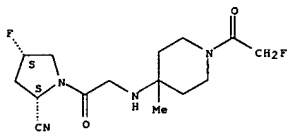


RN 651056-19-8 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(fluoroacetyl)-4-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-18-7
CMF C15 H22 F2 N4 O2

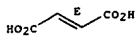
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



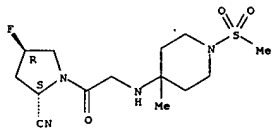
RN 651056-21-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-methyl-1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2S,4R)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-20-1
CMF C14 H23 F N4 O3 S

Absolute stereochemistry.

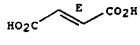
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

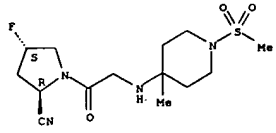


RN 651056-24-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-methyl-1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2R,4S)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-23-4
CMF C14 H23 F N4 O3 S

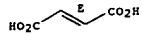
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

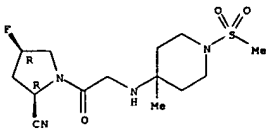


L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 651056-27-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-methyl-1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2R,4R)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-26-7
CMF C14 H23 F N4 O3 S

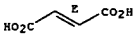
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



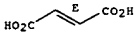
RN 651056-30-3 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2S,4R)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(hydroxyacetyl)-4-methyl-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-29-0
CMF C15 H23 F N4 O3

Absolute stereochemistry.

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

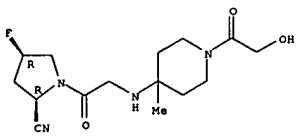


RN 651056-36-9 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2R,4R)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(hydroxyacetyl)-4-methyl-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-35-8
CMF C15 H23 F N4 O3

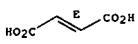
Absolute stereochemistry.



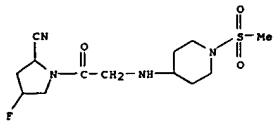
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

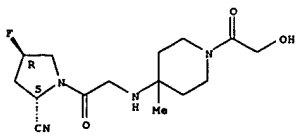


RN 651057-02-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]- (9CI) (CA INDEX NAME)



RN 651057-03-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-methyl-1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]- (9CI) (CA INDEX NAME)

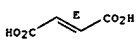
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

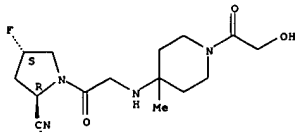


RN 651056-33-6 HCAPLUS
CN 4-Piperidinamine, N-[2-[(2R,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]-1-(hydroxyacetyl)-4-methyl-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 651056-32-5
CMF C15 H23 F N4 O3

Absolute stereochemistry.

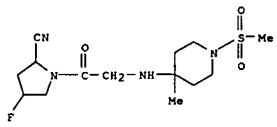


CM 2

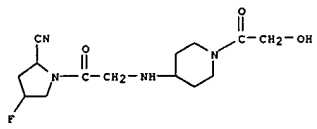
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

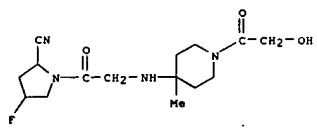
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



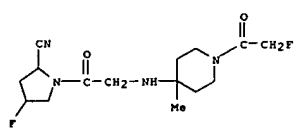
RN 651057-04-4 HCAPLUS
CN 4-Piperidinamine, N-[2-(2-cyano-4-fluoro-1-pyrrolidinyl)-2-oxoethyl]-1-(hydroxyacetyl)- (9CI) (CA INDEX NAME)



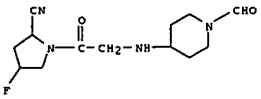
RN 651057-05-5 HCAPLUS
CN 4-Piperidinamine, N-[2-(2-cyano-4-fluoro-1-pyrrolidinyl)-2-oxoethyl]-1-(hydroxyacetyl)-4-methyl- (9CI) (CA INDEX NAME)



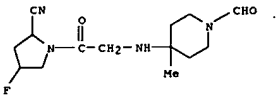
RN 651057-06-6 HCAPLUS
CN 4-Piperidinamine, N-[2-(2-cyano-4-fluoro-1-pyrrolidinyl)-2-oxoethyl]-1-(fluoroacetyl)-4-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 651057-07-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(1-formyl-4-piperidinyl)amino]acetyl]- (9CI) (CA INDEX NAME)

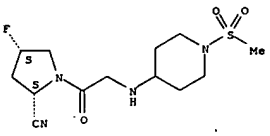


RN 651057-08-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(1-formyl-4-methyl-4-piperidinyl)amino]acetyl]- (9CI) (CA INDEX NAME)



RN 651057-09-9 HCAPLUS
CN Morpholine, 4-[[4-[[2-(2-cyano-4-fluoro-1-pyrrolidinyl)-2-oxoethyl]amino]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

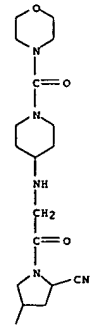
L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

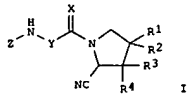
IT 651054-97-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (cyano)(fluoro)pyrrolidine derivs. as dipeptidylpeptidase (DPP) IV inhibitors)
RN 651054-97-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-(methylsulfonyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 30 Jan 2004
ACCESSION NUMBER: 2004:76522 HCAPLUS
DOCUMENT NUMBER: 140:122807
TITLE: Dipeptidyl peptidase IV (DPPIV) inhibitors containing cyanopyrrolidines and their use as antidiabetic agents
INVENTOR(S): Fukushima, Hiroshi; Hiradate, Akira; Takahashi, Masato; Kameo, Kazuya
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 54 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004026820	A	20040129	JP 2003-130830	20030508
PRIORITY APPLN. INFO.:			JP 2002-134420 A	20020509

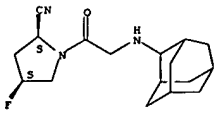
OTHER SOURCE(S): MARPAT 140:122807
GI



AB Title inhibitors contain cyanopyrrolidines I [R1 = halo, OH, C1-5 alkoxy, C1-5 alkyl; R2-R4 = H, halo, OH, C1-5 alkoxy, C1-5 alkyl; R1R2 and/or R3R4 may be O, hydroxyimino, C1-5 alkoxyimino, C1-5 alkylidene; X = O, S; Y = CR5R6, CR7R8CR9R10; R5-R10 = H, halo, (un)substituted C1-10 alkyl, etc.; Z = H, halo, OH, C1-5 hydroxyalkyl, SH, (un)substituted Ph, imidazolyl, indolyl, etc.] or their pharmacol. acceptable salts. Thus, (2S,4S)-2-aminocarbonyl-4-fluoropyrrolidine HCl salt was amidated with (2S,3S)-2-fluorenylmethoxycarbonylamino-3-methylpentanoic acid, treated with trifluoroacetic anhydride, deprotected, and converted into HCl salt to give (2S,4S)-1-[(2S,3S)-2-amino-3-methylpentanoyl]-2-cyano-4-fluoropyrrolidine HCl salt, which inhibited DPPIV with IC50 value of 0.6 nM.
IT 426844-01-1P 426844-02-2P 426844-03-3P
426844-04-4P 428508-72-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyanopyrrolidines as dipeptidyl peptidase IV inhibitors for
treatment of diabetes)
RN 426844-01-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[(tricyclo[3.3.1.13,7]dec-2-ylamino)acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

L4 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

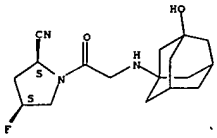
Absolute stereochemistry.



● HCl

RN 426844-02-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

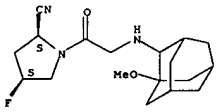


● HCl

RN 426844-03-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(3-methoxytricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

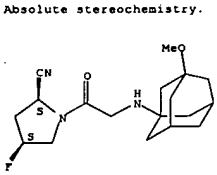


● HCl

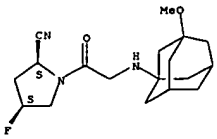
IT 648908-74-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyanopyrrolidines as dipeptidyl peptidase IV inhibitors for treatment of diabetes)

RN 648908-74-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(3-methoxytricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



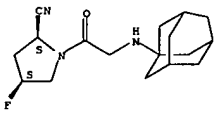
L4 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● HCl

RN 426844-04-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[(tricyclo[3.3.1.13,7]dec-1-ylamino)acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 428508-72-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(1-methoxytricyclo[3.3.1.13,7]dec-2-yl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

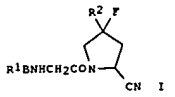
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 14 Sep 2003
ACCESSION NUMBER: 2003:719461 HCAPLUS
DOCUMENT NUMBER: 139:245893
TITLE: Preparation of aminoacetylpyrrolidinecarbonitriles as inhibitors of DPP-IV
INVENTOR(S): Aranyi, Peter; Balazs, Laszlo; Bata, Imre; Batori, Sandor; Boronkay, Eva; Bovy, Philippe; Kanai, Karoly; Kapui, Zoltan; Susan, Edit; Szabo, Tibor; Nagy, Lajos T.; Urban-Szabo, Katalin; Varga, Marton
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.; et al.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

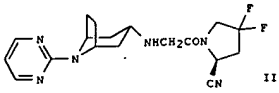
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074500	A2	20030912	WO 2003-HU17	20030304
WO 2003074500	A3	20031218		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 200200849	A2	20040830	HU 2002-849	20020306
CA 2475312	A1	20030912	CA 2003-2475312	20030304
AU 2003209514	A1	20030916	AU 2003-209514	20030304
EP 1487807	A2	20041222	EP 2003-743452	20030304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007960	A	20050215	BR 2003-7960	20030304
US 2005130981	A1	20050616	US 2003-507005	20030304
CN 1639159	A	20050713	CN 2003-805263	20030304
JP 2005529078	T	20050929	JP 2003-572969	20030304
TW 250978	B	20060311	TW 2003-92104743	20030306
IN 2004KN01079	A	20060127	IN 2004-KN1079	20040728
ZA 2004006467	A	20050622	ZA 2004-6467	20040813
NO 2004004221	A	20041206	NO 2004-4221	20041005
PRIORITY APPLN. INFO.:			HU 2002-849 A	20020306
			WO 2003-HU17 W	20030304

OTHER SOURCE(S): MARPAT 139:245893
GI

Appl.

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



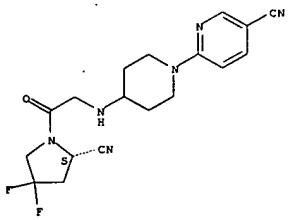


AB Title compds. I [R1 = (un)substituted N heteroarom., thienyl, furyl, CH2Ph, tosyl, acyl; B = N heterocyclic; R2 = H, F] were prepared for use as dipeptidyl peptidase IV (DPP-IV) inhibitors with IC50 ≤ 100 nM, useful in the treatment of diabetes. Thus, the title compound II was prepared from 8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl-exo-amine and (2S)-1-chloroacetyl-4,4-difluoro-2-pyrrolidinecarbonitrile, each prepared in several steps.

IT 596816-23-8P 596816-24-9P 596816-25-0P
596816-26-1P 596816-27-2P 596816-28-3P
596816-29-4P 596816-30-7P 596816-31-8P
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596816-35-2P 596816-36-3P 596816-37-4P
596816-38-5P 596816-39-6P 596816-40-9P
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596816-44-3P 596816-45-4P 596816-46-5P
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596816-54-5P 596816-56-7P 596816-59-0P
596816-61-4P 596816-63-6P 596816-65-8P
596816-67-0P 596816-69-2P 596816-70-5P
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596816-83-0P 596816-84-1P 596816-85-2P
596816-86-3P 596816-87-4P 596816-88-5P
596816-89-6P 596816-90-9P 596816-91-0P
596816-92-1P 596816-93-2P 596816-94-3P
596816-95-4P 596816-96-5P 596816-97-6P
596816-98-7P 596818-14-3P 596818-15-4P
596818-16-5P 596818-17-6P 596818-18-7P
599165-24-9P 599165-25-0P 599165-26-1P
599165-36-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

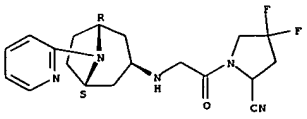
Absolute stereochemistry.



●2 HCl

RN 596816-26-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



●2 HCl

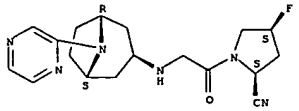
RN 596816-27-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
study); PREP (Preparation); USES (Uses)
(prepn. of aminoacetylpyrrolidinecarbonitriles as inhibitors of DPP-IV)

RN 596816-23-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

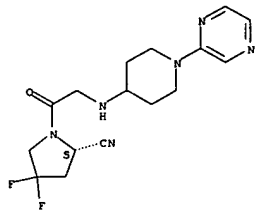
Absolute stereochemistry.



●2 HCl

RN 596816-24-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[(1-pyrazinyl-4-piperidinyl)amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

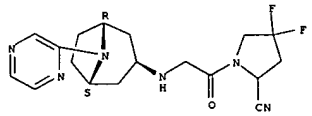
Absolute stereochemistry.



●2 HCl

RN 596816-25-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-2-pyridinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

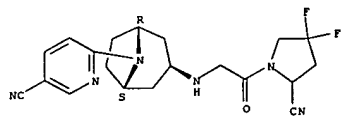
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 596816-28-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

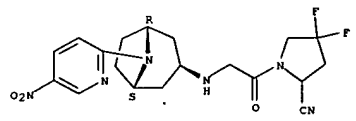
Relative stereochemistry.



●2 HCl

RN 596816-29-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

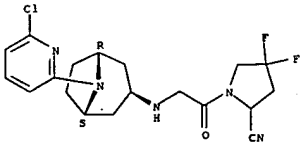
Relative stereochemistry.



RN 596816-30-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

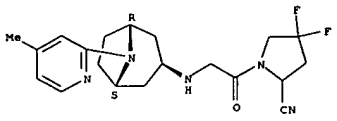
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 596816-31-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(4-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



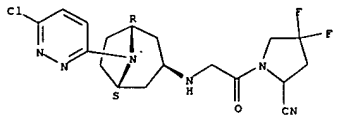
●3 HCl

RN 596816-32-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

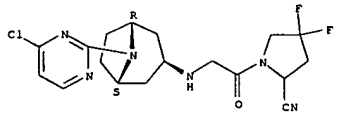
Relative stereochemistry.



●2 HCl

RN 596816-36-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(4-chloro-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

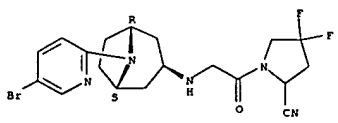


●2 HCl

RN 596816-37-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloropyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

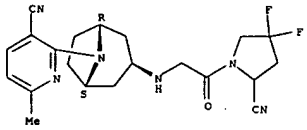
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 596816-33-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

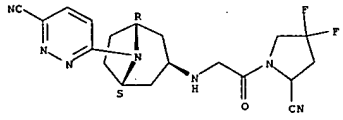
Relative stereochemistry.



●2 HCl

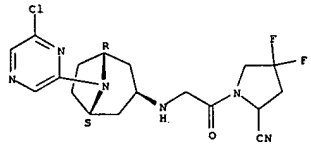
RN 596816-34-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-cyano-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 596816-35-2 HCAPLUS

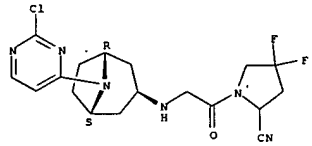
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 596816-38-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(2-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

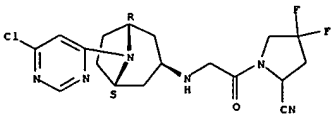


●2 HCl

RN 596816-39-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

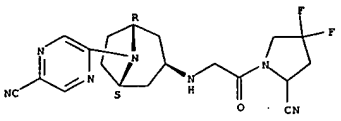
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 596816-40-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, hydrochloride (2:3) (9CI) (CA INDEX NAME)

Relative stereochemistry.

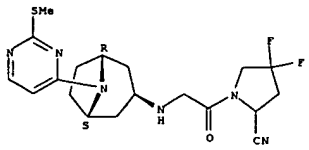


●3/2 HCl

RN 596816-41-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-[2-(methylthio)-4-pyrimidinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

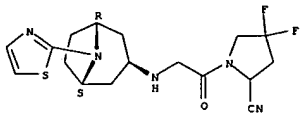
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

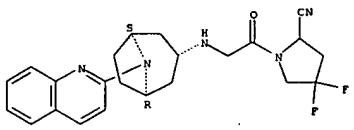
RN 596816-42-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-thiazolyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 596816-43-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-quinolinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

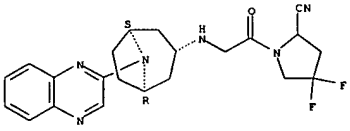


●3 HCl

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 596816-44-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-quinoxalinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

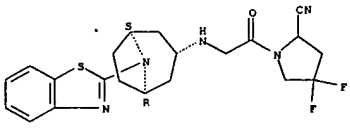
Relative stereochemistry.



●2 HCl

RN 596816-45-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(2-benzothiazolyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

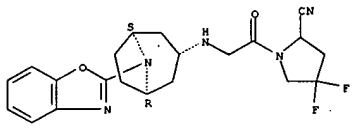


●2 HCl

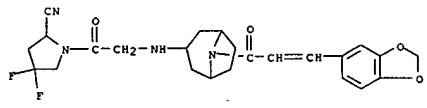
RN 596816-46-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(2-benzoxazolyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

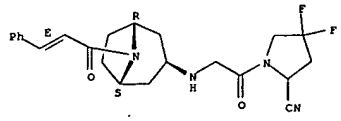


RN 596816-47-6 HCAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-[(2E)-3-(1,3-benzodioxol-5-yl)-1-oxo-2-propenyl]-N-[2-(2-cyano-4,4-difluoro-1-pyrrolidinyl)-2-oxoethyl]-, (3-exo)- (9CI) (CA INDEX NAME)



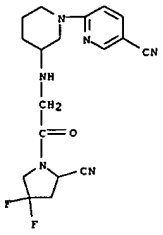
RN 596816-48-7 HCAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-(2-cyano-4,4-difluoro-1-pyrrolidinyl)-2-oxoethyl]-8-[(2E)-1-oxo-3-phenyl-2-propenyl]-, (3-exo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



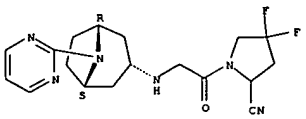
RN 596816-49-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-2-pyridinyl)-3-piperidinyl]amino]acetyl]-4,4-difluoro- (9CI) (CA INDEX NAME)

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 596816-51-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-endo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

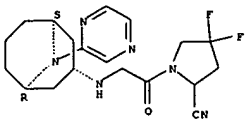
Relative stereochemistry.



RN 596816-52-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-9-pyrazinyl-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

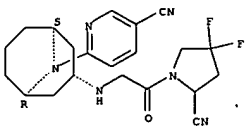
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● 2 HCl

RN 596816-53-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

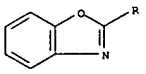


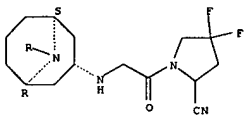
● 2 HCl

RN 596816-54-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-9-(2-benzoxazolyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-4,4-difluoro-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

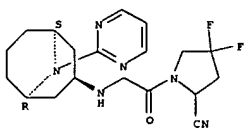




● HCl

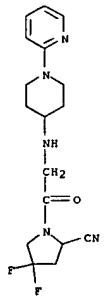
RN 596816-56-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



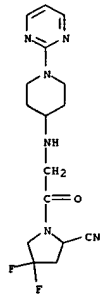
RN 596816-59-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● 2 HCl

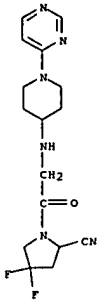
RN 596816-61-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(2-pyrimidinyl)-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

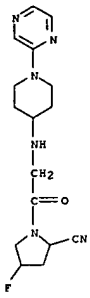
RN 596816-63-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(4-pyrimidinyl)-4-piperidinyl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



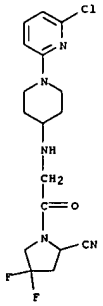
●3 HCl

RN 596816-65-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(1-pyrazinyl-4-piperidinyl)amino]acetyl]- (9CI) (CA INDEX NAME)



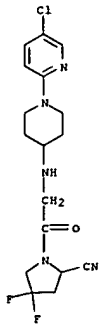
RN 596816-67-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(5-methyl-2-pyridinyl)-4-piperidinyl]amino]acetyl]-, hydrochloride (2:5) (9CI) (CA INDEX NAME)

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(6-chloro-2-pyridinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)



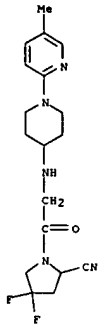
●2 HCl

RN 596816-71-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-chloro-2-pyridinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)



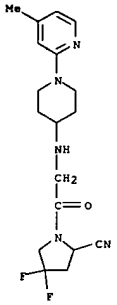
●2 HCl

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●5/2 HCl

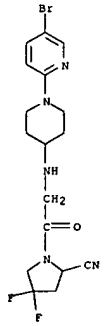
RN 596816-69-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(4-methyl-2-pyridinyl)-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

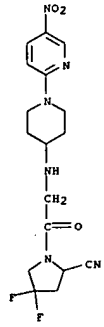
RN 596816-70-5 HCAPLUS

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 596816-72-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-bromo-2-pyridinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

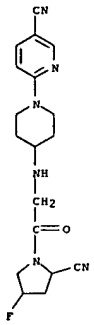
RN 596816-73-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(5-nitro-2-pyridinyl)-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

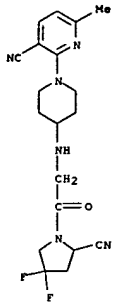
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 596816-74-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-2-pyridinyl)-4-piperidinyl]amino]acetyl]-4-fluoro- (9CI) (CA INDEX NAME)



RN 596816-75-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(3-cyano-6-methyl-2-pyridinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

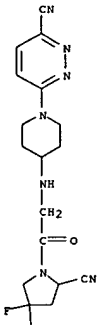
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 596816-76-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(6-cyano-3-pyridazinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro- (9CI) (CA INDEX NAME)

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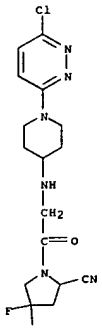


L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

RN 596816-77-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(6-chloro-3-pyridazinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

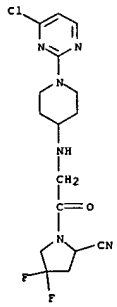


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●2 HCl

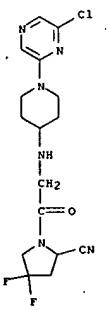
RN 596816-78-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(4-chloro-2-pyrimidinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

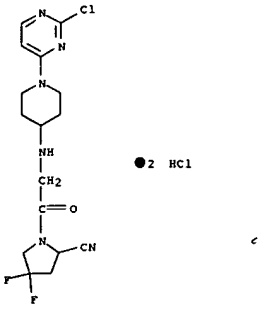
RN 596816-79-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(6-chloropyrazinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

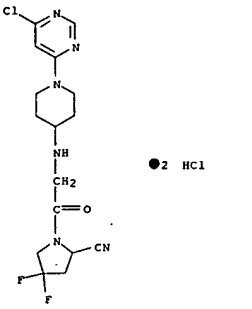
RN 596816-80-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(2-chloro-4-pyrimidinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●2 HCl

RN 596816-81-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(6-chloro-4-pyrimidinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

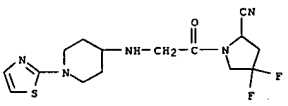


●2 HCl

RN 596816-82-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyanopyrazinyl)-4-

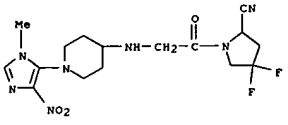
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 596816-84-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(2-thiazolyl)-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



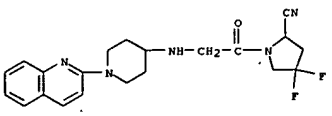
●2 HCl

RN 596816-85-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(1-methyl-4-nitro-1H-imidazol-5-yl)-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

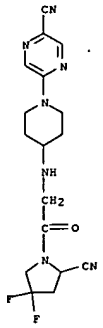
RN 596816-86-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(2-quinolinyl)-4-piperidinyl]amino]acetyl]-, hydrochloride (2:5) (9CI) (CA INDEX NAME)



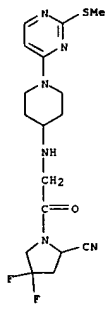
●5/2 HCl

RN 596816-87-4 HCAPLUS

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
piperidinyl]amino]acetyl]-4,4-difluoro- (9CI) (CA INDEX NAME)

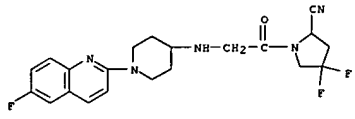


RN 596816-83-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-[2-(methylthio)-4-pyrimidinyl]-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



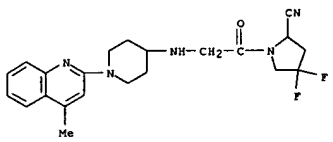
●2 HCl

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(6-fluoro-2-quinolinyl)-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



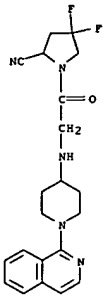
●2 HCl

RN 596816-88-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(4-methyl-2-quinolinyl)-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



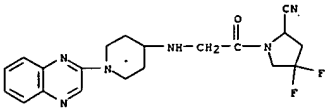
●2 HCl

RN 596816-89-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(1-isoquinolinyl)-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



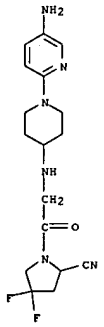
●2 HCl

RN 596816-90-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(2-quinoxalinyl)-4-piperidinyl]amino]acetyl]-, hydrochloride (2:5) (9CI) (CA INDEX NAME)



●5/2 HCl

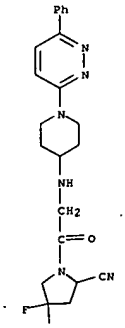
RN 596816-91-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(2-benzothiazolyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

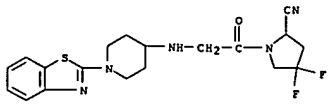


●3 HCl

RN 596816-94-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(6-phenyl-3-pyridazinyl)-4-piperidinyl]amino]acetyl]- (9CI) (CA INDEX NAME)

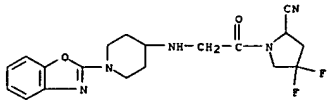
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●2 HCl

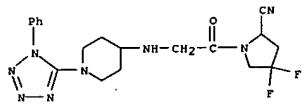
RN 596816-92-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(2-benzoxazolyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro- (9CI) (CA INDEX NAME)



RN 596816-93-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-amino-2-pyridinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, trihydrochloride (9CI) (CA INDEX NAME)

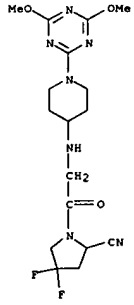
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RN 596816-95-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-(1-phenyl-1H-tetrazol-5-yl)-4-piperidinyl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 596816-96-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

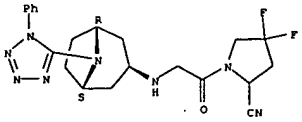


●2 HCl

RN 596816-97-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(1-phenyl-1H-tetrazol-5-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

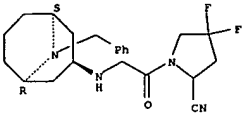
Relative stereochemistry.



●2 HCl

RN 596816-98-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-endo)-9-(phenylmethyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)

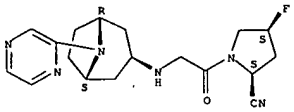
Relative stereochemistry.



●3 HCl

RN 596818-14-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

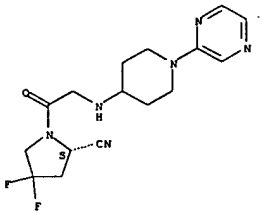
Absolute stereochemistry.



RN 596818-15-4 HCAPLUS

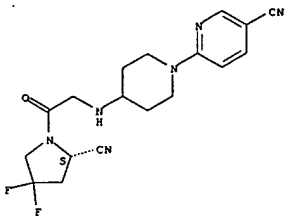
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[(1-pyrazinyl-4-piperidinyl)amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 596818-16-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-2-pyridinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, (2S)- (9CI) (CA INDEX NAME)

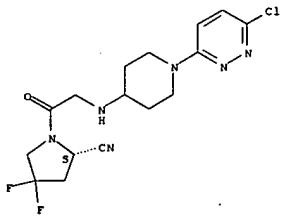
Absolute stereochemistry.



RN 596818-17-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(6-chloro-3-pyridazinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, (2S)- (9CI) (CA INDEX NAME)

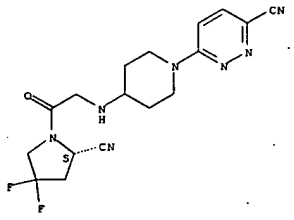
Absolute stereochemistry.

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 596818-18-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(6-cyano-3-pyridazinyl)-4-piperidinyl]amino]acetyl]-4,4-difluoro-, (2S)- (9CI) (CA INDEX NAME)

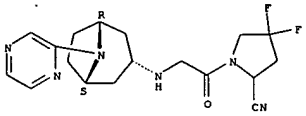
Absolute stereochemistry.



RN 599165-24-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-endo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

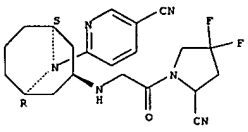
L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



●3 HCl

RN 599165-25-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-endo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

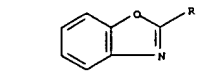


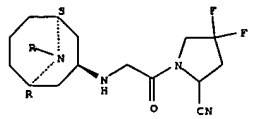
●2 HCl

RN 599165-26-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-endo)-9-(2-benzoxazolyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

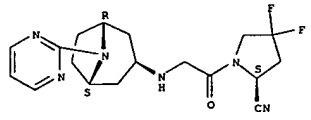




●2 HCl

RN 599165-36-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 18 Jul 2003
ACCESSION NUMBER: 2003:551490 HCAPLUS
DOCUMENT NUMBER: 139:101423
TITLE: Preparation of 2-pyrrolidinecarbonitrile derivatives and related compounds as inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Belyakov, Sergei; Hamilton, Gregory S.; Hurst, David Chadwick; Kalish, Vincent J.; Li, Weixing; Wang, Eric; Wilkinson, Douglas; Wu, Yong-Qian; Xu, Weizheng
PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003057666	A2	20030717	WO 2002-US41469		20021226
WO 2003057666	A3	20031211			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2471204	A1	20030717	CA 2002-2471204		20021226
AU 2002367395	A1	20030724	AU 2002-367395		20021226
EP 1465891	A2	20041013	EP 2002-806232		20021226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005523248	T	20050804	JP 2003-557983		20021226
US 2005070719	A1	20050331	US 2004-499675		20041101
			US 2001-342092P	P	20011226
			US 2002-407947P	P	20020905
			WO 2002-US41469	W	20021226

PRIORITY APPLN. INFO.:
OTHER SOURCE(S): MARPAT 139:101423
GI

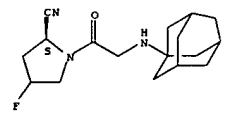
L4 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I

AB 2-Pyrrolidinecarbonitrile derivs. and related compds., e.g., I or unsatd. analogs [X is CH2, CH, S, O, NH, N, CO, CF2, CF, CH-Y, or C-Y; Z is CH2, CH, CF2, CF, C-Y or CH-Y (Y is halo, OH, or alkyloxy; one of X or Z must be CH2 or CH); G is (fused) 2-pyrrolidinyl or 2-piperidinyl], were prepared as inhibitors of dipeptidyl peptidase IV (DPP IV) for the treatment of neurol. disorders, diabetes, inflammatory disorders, and other diseases. Thus, 2-cyano-4-fluoro-1-(cyclohexylglycyl)pyrrolidine hydrochloride was prepared via peptide coupling reaction and showed IC50 = 6.5 nM for inhibition of DPP IV.
IT 556835-00-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidinecarbonitrile derivs. and related compds. as inhibitors of dipeptidyl peptidase IV)
RN 556835-00-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[(tricyclo[3.3.1.13,7]dec-1-ylamino)acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

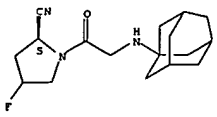
L4 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 18 Jul 2003
ACCESSION NUMBER: 2003:551318 HCAPLUS
DOCUMENT NUMBER: 139:97270
TITLE: Inhibitors of dipeptidyl peptidase IV and methods for treating neurological and other diseases
INVENTOR(S): Belyakov, Sergei; Hamilton, Gregory S.; Li, Weixing; Xu, William; Hurst, David Chadwick; Kalish, Vincent J.; Wu, Yong-Qian; Wang, Eric; Wilkinson, Douglas
PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003057144	A2	20030717	WO 2002-US41134		20021224
WO 2003057144	A3	20040226			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002360732	A1	20030724	AU 2002-360732		20021224
			US 2001-342092P	P	20011226
			US 2002-407947P	P	20020905
			WO 2002-US41134	W	20021224

PRIORITY APPLN. INFO.:
OTHER SOURCE(S): MARPAT 139:97270
AB Novel inhibitors of dipeptidyl peptidase IV (DPP IV; EC 3.4.14.5), such as N-substituted cyanopyrrolidine compds., pharmaceutical compns. comprising therapeutically effective amts. of such inhibitors, and novel methods of treating medical conditions are provided. The novel inhibitors of DPP IV described herein are useful in the treatment of neurol. disorders, diabetes, inflammatory disorders such as arthritis, obesity, osteoporosis, and of such other enumerated conditions as can be treated with inhibitors of DPP IV. Thus, many potential DPP IV inhibitors were synthesized. One such compound, 2-cyano-4-fluoro-1-(octahydroindole-2-carbonyl)pyrrolidine HCl, was found to inhibit DPP IV in vitro, with IC50 6.2 nM. Such compds. also protected neurons in spinal cord slices from the neurotoxin L-(-)-threo-3-hydroxyaspartic acid.
IT 556835-00-8P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors of dipeptidyl peptidase IV and methods for treating neurol.

L4 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
and other diseases)
RN 556835-00-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[(tricyclo[3.3.1.13,7]dec-1-ylamino)acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

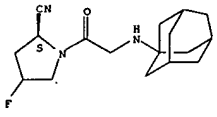
Absolute stereochemistry.



● HCl

IT 557771-18-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of dipeptidyl peptidase IV and methods for treating neurol.
and other diseases)
RN 557771-18-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[(tricyclo[3.3.1.13,7]dec-1-ylamino)acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

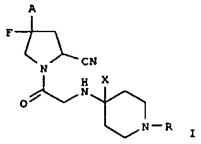


L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 10 Jan 2003
ACCESSION NUMBER: 2003:22868 HCAPLUS
DOCUMENT NUMBER: 138:90072
TITLE: Preparation of fluoropyrrolidinecarbonitrile derivatives as dipeptidyl peptidase inhibitors
INVENTOR(S): Haffner, Curt Dale; McDougald, Darryl Lynn; Lenhard, James Martin
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003002553	A2	20030109	WO 2002-US20470	20020626
WO 2003002553	A3	20030327		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1399433	A2	20040324	EP 2002-742328	20020626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005500321	T	20050106	JP 2003-508934	20020626
ZA 2003009170	A	20050225	ZA 2003-9170	20031125
US 2004242636	A1	20041202	US 2003-481543	20031219
JP 2006306886	A	20061109	JP 2006-177193	20060627
PRIORITY APPLN. INFO.:			US 2001-301333P	P 20010627
			US 2002-384041P	P 20020529
			US 2002-376015P	P 20020426
			JP 2003-508714	A3 20020626
			WO 2002-US20470	W 20020626

OTHER SOURCE(S): MARPAT 138:90072
GI

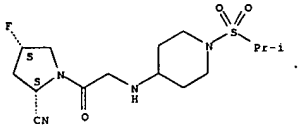
L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



AB Novel compds. I [X = H or alkyl; R = isopropyl-, benzyl-, naphthylethyl-, or mesitylsulfonyl, (un)substituted cycloalkylsulfonyl or aryl, benzoxazolyl; A undefined] were prepared for inhibiting serine proteases such as dipeptidyl peptidases (e.g., DPP-IV). Thus, (2S,4S)-4-fluoro-1-[[[1-(isopropylsulfonyl)-4-piperidinyl]amino]acetyl]-2-pyrrolidinecarbonitrile hydrochloride was prepared by alkylation of 1-(isopropylsulfonyl)-4-piperidinamine hydrochloride (preparation given) with
(2S,4S)-1-(bromoacetyl)-4-fluoro-2-pyrrolidinecarbonitrile.
IT 483365-63-5P 483365-64-6P 483365-67-9P
483365-68-0P 483365-69-1P 483365-70-4P
483365-71-5P 483365-72-6P 483365-73-7P
483365-74-8P 483365-75-9P 483365-76-0P
483365-80-6P 483365-81-7P 483365-82-8P
483365-83-9P 483365-84-0P 483365-85-1P
483365-86-2P 483365-93-1P 483365-94-2P
483365-95-3P 483365-98-6P 483365-99-7P
483366-00-3P 483366-01-4P 483366-02-5P
483366-03-6P 483366-04-7P 483366-06-9P
483366-07-0P 483366-08-1P 483366-99-0P
483973-61-1P 483973-62-2P 483973-63-3P
483973-64-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fluoropyrrolidinecarbonitrile derivs. as dipeptidyl peptidase inhibitors)
RN 483365-63-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[(1-methylethyl)sulfonyl]-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

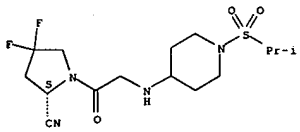
L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● HCl

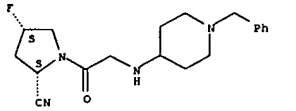
RN 483365-64-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-[(1-methylethyl)sulfonyl]-4-piperidinyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 483365-67-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-(phenylmethyl)-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

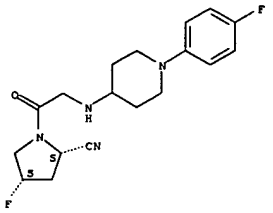
Absolute stereochemistry.



● HCl

RN 483365-68-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-(4-fluorophenyl)-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

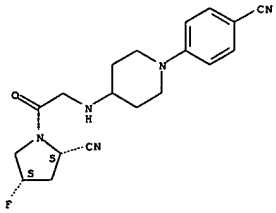
L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



● HCl

RN 483365-69-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(4-cyanophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

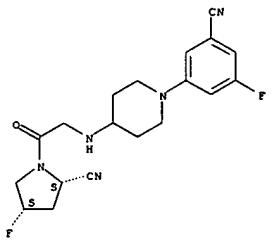


● HCl

RN 483365-70-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(4-cyano-3-fluorophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(3-cyano-5-fluorophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

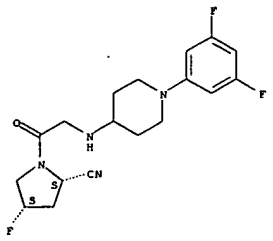
Absolute stereochemistry.



● HCl

RN 483365-73-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(3,5-difluorophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

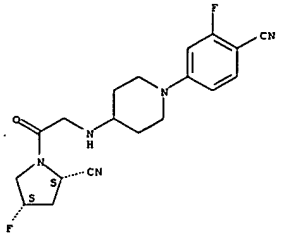
Absolute stereochemistry.



● HCl

RN 483365-74-8 HCAPLUS

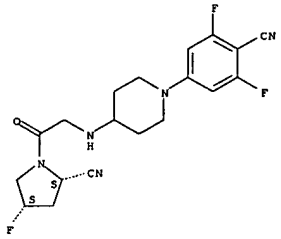
L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



● HCl

RN 483365-71-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(4-cyano-3,5-difluorophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

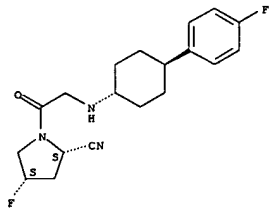


● HCl

RN 483365-72-6 HCAPLUS

L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-4-(4-fluorophenyl)cyclohexyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

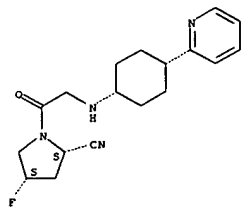
Absolute stereochemistry.



● HCl

RN 483365-75-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[cis-4-(2-pyridinyl)cyclohexyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

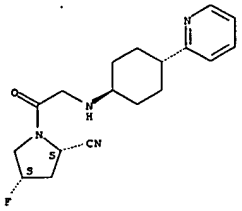
Absolute stereochemistry.



● HCl

RN 483365-76-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[trans-4-(2-pyridinyl)cyclohexyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

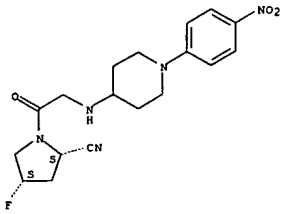
L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



● HCl

RN 483365-80-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-(4-nitrophenyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

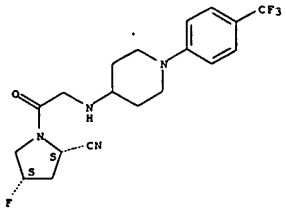
Absolute stereochemistry.



RN 483365-81-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[4-(trifluoromethyl)phenyl]-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

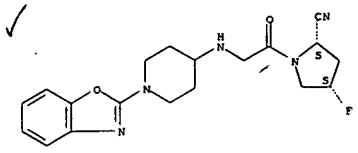
L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● HCl

RN 483365-82-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(2-benzoxazolyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

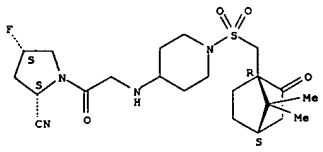


● HCl

RN 483365-83-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-[[[(1R,4S)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]methyl]sulfonyl]-4-piperidinyl]amino]acetyl]-4-fluoro-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

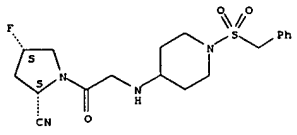
L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● HCl

RN 483365-84-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[(phenylmethyl)sulfonyl]-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

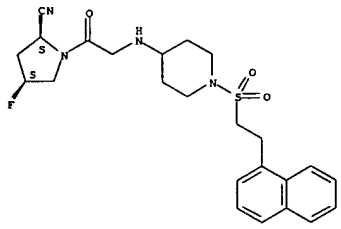


● HCl

RN 483365-85-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[[2-(1-naphthalenyl)ethyl]sulfonyl]-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

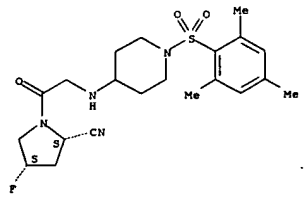
L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● HCl

RN 483365-86-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[(2,4,6-trimethylphenyl)sulfonyl]-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

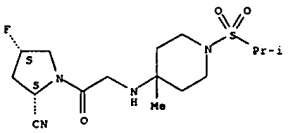


● HCl

RN 483365-93-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-methyl-1-[(1-methylethyl)sulfonyl]-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

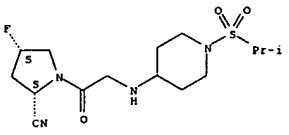
L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● HCl

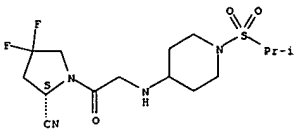
RN 483365-94-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[(1-methylethyl)sulfonyl]-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



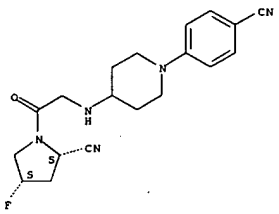
RN 483365-95-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[1-[(1-methylethyl]sulfonyl]-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



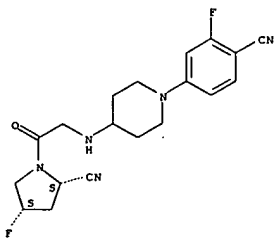
● HCl

L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 483366-01-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(4-cyano-3-fluorophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

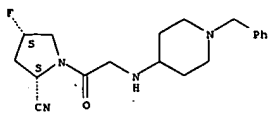


RN 483366-02-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(4-cyano-3,5-difluorophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

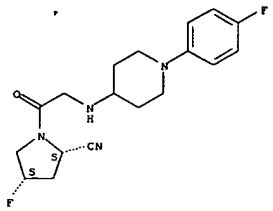
L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 483365-98-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-(phenylmethyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 483365-99-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-(4-fluorophenyl)-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

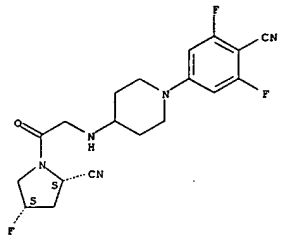
Absolute stereochemistry.



RN 483366-00-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(4-cyanophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

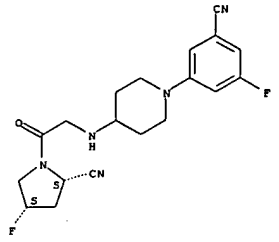
Absolute stereochemistry.

L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 483366-03-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(3-cyano-5-fluorophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

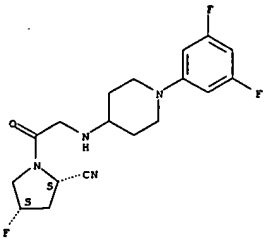
Absolute stereochemistry.



RN 483366-04-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(3,5-difluorophenyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

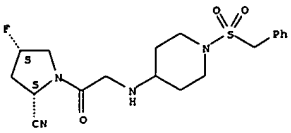
Absolute stereochemistry.

L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 483366-06-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[(phenylmethyl)sulfonyl]-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

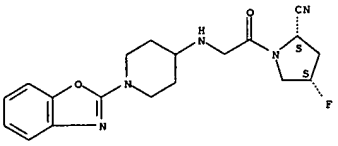
Absolute stereochemistry.



RN 483366-07-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[[2-(1-naphthalenyl)ethyl]sulfonyl]-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

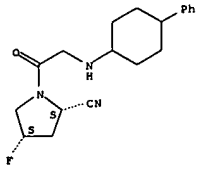
Absolute stereochemistry.

L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 483973-61-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(4-phenylcyclohexyl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

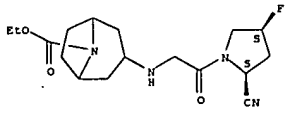
Absolute stereochemistry.



● HCl

RN 483973-62-2 HCAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-carboxylic acid, 3-[[2-[(2S,4S)-2-cyano-4-fluoro-1-pyrrolidinyl]-2-oxoethyl]amino]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

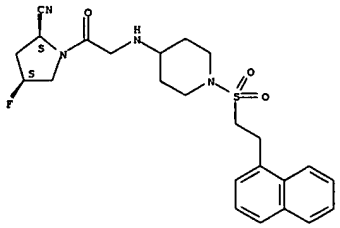
Absolute stereochemistry.



● HCl

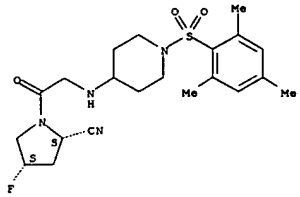
RN 483973-63-3 HCAPLUS

L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 483366-08-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[1-[(2,4,6-trimethylphenyl)sulfonyl]-4-piperidinyl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

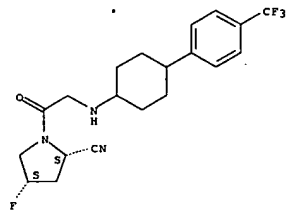


RN 483366-99-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(2-benzoxazolyl)-4-piperidinyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[4-[4-(trifluoromethyl)phenyl]cyclohexyl]amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

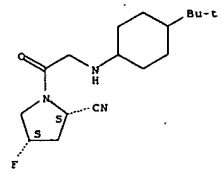
Absolute stereochemistry.



● HCl

RN 483973-64-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[4-(1,1-dimethylethyl)cyclohexyl]amino]acetyl]-4-fluoro-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

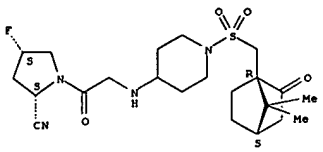


● HCl

IT 483366-77-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of fluoropyrrolidinecarbonitrile derivs. as dipeptidyl peptidase inhibitors)
RN 483366-77-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-[[[(1R,4S)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]methyl]sulfonyl]-4-piperidinyl]amino]acetyl]-4-

L4 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 16 May 2002
ACCESSION NUMBER: 2002:368450 HCAPLUS
DOCUMENT NUMBER: 136:386016
TITLE: Preparation of 2-cyanopyrrolidine derivatives as dipeptidyl peptidase IV (DPPIV) inhibitors
INVENTOR(S): Fukushima, Hiroshi; Hiratate, Akira; Takahashi, Masato; Kameo, Kazuya
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

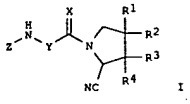
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WO 2002038541	A1	20020516	WO 2001-JP9818	20011109
WO 2002038541	A9	20020808		
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EP 1333025	A1	20030806	EP 2001-981047	20011109
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CN 1474809	A	20040211	CN 2001-818732	20011109
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NO 2003001949	A	20030708	NO 2003-1949	20030429
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PRIORITY APPLN. INFO.:
JP 2000-344036 A 20001110
JP 2001-215766 A 20010716

L4 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CA 2001-2428271	A3	20011109
CN 2001-818732	A3	20011109
EP 2001-981047	A3	20011109
WO 2001-JP9818	W	20011109

OTHER SOURCE(S): MARPAT 136:386016
GI



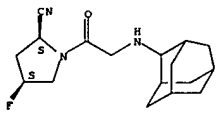
AB Cyanopyrrolidine derivs. represented by the general formula (I) or pharmaceutically acceptable salts thereof [wherein R1 is halogeno, hydroxyl, C1-5 alkoxy, or C1-5 alkyl or, and R2 is hydrogen, halogeno, hydroxyl, C1-5 alkoxy, or C1-5 alkyl or alternatively R1 and R2 are united to form oxo, hydroxyimino, C1-5 alkoxyimino, or C1-5 alkylidene; R3 and R4 are each hydrogen, halogeno, hydroxyl, C1-5 alkoxy, or C1-5 alkyl or alternatively R3 and R4 are united to form oxo, hydroxyimino, C1-5 alkoxyimino, or C1-5 alkylidene; X is oxygen or sulfur; Y is CR5R6 (wherein R5 and R6 are each independently hydrogen, halogeno, or the like) or CR7R8CR9R10 (wherein R7, R8, R9, and R10 are each independently hydrogen, halogeno, or the like, or alternatively R7 and R9 together with the carbon atoms adjacent thereto form C3-8 cycloalkyl or the like); and Z is hydrogen or optionally substituted C1-10 alkyl, or alternatively Y and Z together with the nitrogen atom adjacent thereto form optionally substituted cyclic C2-10 amino] are prepared These compds. are useful for the prevention or treatment of diabetes and immune diseases. Thus, N-acylation of (2S,4S)-2-(aminocarbonyl)-4-fluoropyrrolidine hydrochloride using 1-hydroxybenzotriazole with (2S,3S)-2-(9-fluorenylmethoxycarbonylamino)-3-methylpentanoic acid with and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in the presence of diisopropylethylamine in DMF/THF at room temperature overnight gave (2S,4S)-2-(aminocarbonyl)-1-[(2S,3S)-2-(9-fluorenylmethoxycarbonylamino)-3-methylpentanoyl]-4-fluoropyrrolidine which was treated with trifluoroacetic anhydride in THF under ice-cooling for 1.5 h to give (2S,4S)-2-cyano-1-[(2S,3S)-2-(9-fluorenylmethoxycarbonylamino)-3-methylpentanoyl]-4-fluoropyrrolidine (II). N-deprotection of II by treatment with diethylamine in 1,2-dichloroethane under ice-cooling for 30 min and at room temperature for 5 h followed by treatment with 4 M HCl/dioxane and purifn. on silica gel column gave (2S,4S)-1-[(2S,3S)-2-amino-3-methylpentanoyl]-2-cyano-4-fluoropyrrolidine hydrochloride (III). III showed IC50 of 0.6 nM against DPPIV.

L4 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

IT 426844-01-1P, (2S,4S)-1-[(2-Adamantylamino)acetyl]-2-cyano-4-fluoropyrrolidine hydrochloride 426844-02-2P, (2S,4S)-2-Cyano-4-fluoro-1-[[(1-hydroxy-3-adamantyl)amino]acetyl]pyrrolidine hydrochloride 426844-03-3P, (2S,4S)-1-[[(1-Methoxy-3-adamantyl)amino]acetyl]-2-cyano-4-fluoropyrrolidine hydrochloride 426844-04-4P, (2S,4S)-1-[(1-Adamantylamino)acetyl]-2-cyano-4-fluoropyrrolidine hydrochloride 428508-72-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-cyanopyrrolidine derivs. as dipeptidyl peptidase IV inhibitors for prevention or treatment of diabetes and immune diseases)

RN 426844-01-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[(tricyclo[3.3.1.13,7]dec-2-ylamino)acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

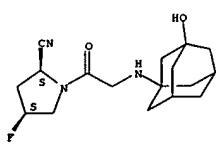
Absolute stereochemistry.



● HCl

RN 426844-02-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

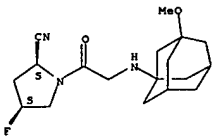
Absolute stereochemistry.



● HCl

L4 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 426844-03-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile,
4-fluoro-1-[[(3-methoxytricyclo[3.3.1.13,7]dec-
1-yl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

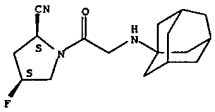
Absolute stereochemistry.



● HCl

RN 426844-04-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[(tricyclo[3.3.1.13,7]dec-1-
ylamino)acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

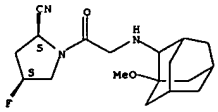


● HCl

RN 428508-72-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile,
4-fluoro-1-[[(1-methoxytricyclo[3.3.1.13,7]dec-
2-yl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	129.01	301.32

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-17.94	-17.94

STN INTERNATIONAL LOGOFF AT 09:56:20 ON 09 FEB 2007